

AWARD/CONTRACT			1. THIS CONTRACT IS A RATED ORDER UNDER DPAS (15 CFR 700)			RATING			PAGE OF PAGES 1 48				
2. CONTRACT (Proc. Inst. Ident.) NO. 75A50120C00154						3. EFFECTIVE DATE See Block 20C			4. REQUISITION/PURCHASE REQUEST/PROJECT NO. OS262624				
5. ISSUED BY CODE ASPR-BARDA  ASPR-BARDA 200 Independence Ave., S.W. Room 640-G Washington DC 20201			6. ADMINISTERED BY (If other than Item 5) CODE ASPR-BARDA  ASPR-BARDA 200 Independence Ave., S.W. Room 638-G Washington DC 20201										
7. NAME AND ADDRESS OF CONTRACTOR (No., street, country, State and ZIP Code)  ESPEROVAX 1562938 Attn: DAVID J OHAGAN 46701 COMMERCE CENTER DR PLYMOUTH MI 481702475						8. DELIVERY <input type="checkbox"/> FOB ORIGIN <input checked="" type="checkbox"/> OTHER (See below)							
						9. DISCOUNT FOR PROMPT PAYMENT							
						10. SUBMIT INVOICES (4 copies unless otherwise specified) TO THE ADDRESS SHOWN IN						ITEM	
CODE 1562938			FACILITY CODE										
11. SHIP TO/MARK FOR CODE HHS/OS/ASPR  HHS/OS/ASPR 200 C St SW WASHINGTON DC 20201			12. PAYMENT WILL BE MADE BY CODE FMS  FMS 7700 Wisconsin Ave Bethesda MD 20814										
13. AUTHORITY FOR USING OTHER THAN FULL AND OPEN COMPETITION <input type="checkbox"/> )						14. ACCOUNTING AND APPROPRIATION DATA 2020.199C014.25106							
15A. ITEM NO		15B. SUPPLIES/SERVICES				15C. QUANTITY		15D. UNIT		15E. UNIT PRICE		15F. AMOUNT	
		Continued											
15G. TOTAL AMOUNT OF CONTRACT										\$606,780.00			
16. TABLE OF CONTENTS													
(X)	SEC.	DESCRIPTION			PAGE(S)	(X)	SEC.	DESCRIPTION			PAGE(S)		
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	B	SUPPLIES OR SERVICES AND PRICES/COSTS				PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACH.							
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CONTRACTING OFFICER WILL COMPLETE ITEM 17 (SEALED-BID OR NEGOTIATED PROCUREMENT) OR 18 (SEALED-BID PROCUREMENT) AS APPLICABLE													
17. <input checked="" type="checkbox"/> CONTRACTOR'S NEGOTIATED AGREEMENT (Contractor is required to sign this document and return _____ copies to issuing office.) Contractor agrees to furnish and deliver all items or perform all the services set forth or otherwise identified above and on any continuation sheets for the consideration stated herein. The rights and obligations of the parties to this contract shall be subject to and governed by the following documents: (a) this award/contract, (b) the solicitation, if any, and (c) such provisions, representations, certifications, and specifications, as are attached or incorporated by reference herein. (Attachments are listed herein.)						18. <input type="checkbox"/> SEALED-BID AWARD (Contractor is not required to sign this document.) Your bid on Solicitation Number _____, including the additions or changes made by you which additions or changes are set forth in full above, is hereby accepted as to the items listed above and on any continuation sheets. This award consummates the contract which consists of the following documents: (a) the Government's solicitation and your bid, and (b) this award/contract. No further contractual document is necessary. (Block 18 should be checked only when awarding a sealed-bid contract.)							
19A. NAME AND TITLE OF SIGNER (Type or print)						20A. NAME OF CONTRACTING OFFICER MATTHEW A. MCCORD							
19B. NAME OF CONTRACTOR ESPEROVAX 1562938					19C. DATE SIGNED		20B. UNITED STATES OF AMERICA				20C. DATE SIGNED		
BY _____ (Signature of person authorized to sign)							BY _____ (Signature of the Contracting Officer)						

# CONTINUATION SHEET

REFERENCE NO. OF DOCUMENT BEING CONTINUED  
75A50120C00154

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NAME OF OFFEROR OR CONTRACTOR

ESPEROVAX 1562938

ITEM NO. (A)	SUPPLIES/SERVICES (B)	QUANTITY (C)	UNIT (D)	UNIT PRICE (E)	AMOUNT (F)
1	<p>Tax ID Number: 83-2601657 DUNS Number: 117307860 Appr. Yr.: 2020 CAN: 199C014 Object Class: 25106 Period of Performance: 07/27/2020 to 10/31/2021</p> <p>Development of mRNA oral cellular vaccine delivery technology.</p> <p>Reports &amp; Other Deliverables Obligated Amount: \$606,780.00</p>				606,780.00

## DRIVE EZ-BAA CONTRACT

### PART I. THE SCHEDULE

#### SECTION A. BACKGROUND

In 2018, the Biomedical Advanced Research and Development Authority (BARDA) established the Division of Research, Innovation, and Venture (DRIVE). The mission of DRIVE is to encourage agile business practices, accelerate biomedical innovations, and improve the availability of transformative products & technologies to protect Americans from natural and intentional health security threats. The following contract and the Statement of Work (addressed in Section C), further the mission and goals of DRIVE.

#### SECTION B. SUPPLIES OR SERVICES AND PRICE/COST

##### B. 1. PRICE

FIRM FIXED PRICE: The firm fixed price of the base period of the contract is \$606,780.

CONTRACT LINE ITEM NO. (CLIN)	PROJECT DESCRIPTION	PERIOD OF PERFORMANCE	QUANTITY	UNIT	UNIT PRICE
0001	COVID-19 Response – development of mRNA oral cellular vaccine delivery technology  Reports & Other Deliverables	27-July-2020 - 31-October-2021	1	JOB	\$606,780

Through negotiations, the Government and Contractor agreed that a total price of \$866,829 would be a realistic and reasonable estimate of Contractor's actual costs of performance. Accordingly, in return for successful completion and delivery of CLIN 0001, the Government's portion will be \$606,780.

##### B. 2. ADVANCE UNDERSTANDINGS

###### a. Sharing of contract deliverables within United States Government (USG)

In an effort to build a robust medical countermeasure pipeline through increased collaboration, the Government may share technical deliverables with Government entities responsible for Medical Countermeasure Development. In accordance with recommendations from the Public Health Emergency Medical Countermeasure Enterprise (PHEMCE) Review, agreements established in the Integrated Portfolio Advisory Committee (PAC) Charter, and agreements between BARDA and the Department of Defense, the National Institutes of Health, the Centers for Disease Control, and the FDA, BARDA may share technical deliverables and test results created in the performance of this Contract with colleagues within the PHEMCE as well as within the Department of Health and Human Services (DHHS). This advance understanding does not authorize the Government to share financial information outside of the United States Government. The Contractor is advised to review the terms of FAR 52.227-14 Rights in Data – General, regarding the Government's rights to data produced during the course of performance of this Contract.

###### b. Approval of Human and Animal Protocols

This contract:

1. ☐ Will or ☒ Will Not include clinical trials (e.g. human protocols); and

2. ☒ **Will** or ☐ **Will Not** include non-clinical trials (e.g. animal protocols).

Accordingly, if checked to indicate either class of studies is *not* included under the subject contract, all of the corresponding clinical and non-clinical clauses, terms, and obligations included in this document are hereby self-deleted.

The Contractor shall submit all human and animal protocols and human informed consent documents as referenced under this Contract to the Contracting Officer (CO) and Contracting Officer's Representative (COR) for review and approval **prior** to seeking other approvals (Institutional Review Board, Human Use Committee, Institutional Animal Care and Use Committee). The Government requires no fewer than eight (8) business days to perform a review. The Contractor shall take this review time into account and submit protocols as early as possible to avoid delays. The Government's comments and feedback shall be addressed prior to approval. The COR will review and provide approval of protocols. Human informed consents shall also be submitted and reviewed with any human protocol.

c. **Rights in Data**

See Section I – Contract Clauses

## **SECTION C. DESCRIPTION/SPECIFICATIONS/WORK STATEMENT**

### **C.1. STATEMENT OF WORK**

See Section J – Attachment 1 (Statement of Work) as agreed upon by the Government and Contractor, and the Reporting Requirements outlined by “DRIVE Digital Resources” accessed via [www.drive.hhs.gov](http://www.drive.hhs.gov).

### **C.2 REGULATORY ACTIVITIES**

The Contractor shall submit to the COR for review and comment, pre-submission documents, submission documents, results documents, and all proposed regulatory filing documents with the FDA.

### **C.3 QUALITY**

The Contractor may be required to establish and maintain a Quality Management System for the proposed effort with sufficient content to include but not limited to the elements contained in the Code of Federal Regulations Title 21 Part 820.

The Contractor may be required to establish routine internal reviews of the proposed effort with documentation and evidence of the ability to maintain, and adhere to the Code of Federal Regulations Title 21 Part 820.

The Contractor may be required to subcontract for an independent audit of its system quality system adherence, resolve any issues noted by the auditor, and provide the audit findings and resolutions to the Government.

## **SECTION D. PACKAGING, MARKING, AND SHIPPING**

All deliverables required under this Contract shall be packaged, marked and shipped in accordance with Government specifications and Section F. At a minimum, all deliverables shall be marked with the contract number and Contractor name. The Contractor shall guarantee that all required materials shall be delivered in immediate usable and acceptable condition.

Unless otherwise specified by the CO, delivery of reports to be furnished to the Government under this Contract (including invoices) shall be delivered to the CO and COR electronically along with a concurrent email notification to the CO and COR (as defined in Section F.3. Electronic Submission) summarizing the electronic delivery.

## **SECTION E. INSPECTION AND ACCEPTANCE**

### **E.1. FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)**

See Section I for a complete list of clauses incorporated by reference.

### **E.2. DESIGNATION OF GOVERNMENT PERSONNEL**

For the purpose of this Section E, the designated COR is the authorized representative of the CO. The COR will assist in resolving technical issues that arise during performance. The COR however is not authorized to change any contract terms or authorize any changes in the Statement of Work, modify or extend the period of performance, or authorize reimbursement of any costs incurred during performance.

### **E.3. INSPECTION, ACCEPTANCE AND CONTRACT MONITORING**

Inspection and acceptance of the product, services, and documentation called for herein shall be accomplished by the CO or a duly authorized representative. Delivery, technical inspection and acceptance will be take place at a location designated by the CO or at:

Office of the Assistant Secretary for Preparedness and Response  
Biomedical Advanced Research and Development Authority  
O'Neill House Office Building  
Washington, DC 20515

At the discretion of the Government and independent of activities conducted by the Contractor, with 48 hours' notice to the Contractor, the Government reserves the right to conduct site visits and inspections related to this Contract on an as needed basis during normal business hours, including collection of product samples and intermediates held at the location of the Contractor, or its subcontractor. All costs reasonably incurred by the Contractor and subcontractor for such visit and/or inspection shall be allowable costs subject to the Allowable cost requirements in FAR Subpart 31.2. The Contractor shall coordinate these visits and shall have the opportunity to accompany the Government on any such visits. Under time-sensitive or critical situations, the Government reserves the right to suspend the 48 hour notice to the Contractor. The areas included under the site visit could include, but are not limited to: security, regulatory and quality systems, manufacturing processes and cGMP/GLP/GCP compliance related to activities funded under this Contract.

If the Government, Contractor, or other party identifies any issues during an audit, the Contractor shall capture the issues, identify potential solutions, and provide a report to the Government for review and acceptance.

- If issues are identified during the audit, the Contractor shall submit a report to the CO and COR within five (5) business days detailing the finding and corrective action(s) of the audit.
- COR and CO will review the report and provide a response to the Contractor within ten (10) business days.
- Once corrective action is completed, the Contractor will provide a final report to the CO and COR.

## **SECTION F. DELIVERIES OR PERFORMANCE**

### **F.1. ESTIMATED PERIOD OF PERFORMANCE**

The estimated period of performance for this Contract shall be consistent with the dates set forth in Section B.2.

### **F.2. DELIVERABLES**

Successful performance under this contract shall be deemed to occur upon completion of performance of the work set forth in Attachment 1 of this contract and upon delivery and acceptance, as required by Attachment 1, by the COR, and of each of the deliverables described in Section C and Section F below.

All deliverables and reporting documents listed within this Section shall be delivered electronically to the CO, the

Contract Specialist (CS), and the COR as well as in the designated eRoom (the Government's SharePoint site) unless otherwise specified by the CO.

Number	Deliverable	Description	Due
1	Work Location Tracking	The Contractor shall submit a detailed spreadsheet regarding locations where work will be performed under this contract, including addresses, points of contact, and work performed per location, to include any subcontractors, if necessary.	Due within 5 business days of award date, and within 30 days after substantive changes are made to locations or capabilities.  Due within 2 business days of a substantive change if the work performed supports medical countermeasure development that addresses a threat that has been declared a Public Health Emergency by the HHS Secretary or a Public Health Emergency of International Concern (PHEIC) by the WHO
2	Kickoff Meeting	The Contractor shall complete a Kickoff meeting after contract award, either as a videoconference or an in-person meeting, to outline activities for the next 30 days.  The Contractor shall provide an itinerary and agenda at least 2 business days in advance of meeting.	Due within 10 days of award date.
3	Project Plan	The Contractor shall submit a detailed Project Plan, Gantt Chart, and Risk Mitigation Plan outlining the goals, deliverables, strategies, and intended pathway for the project.	Due within 10 days of award date.
4	Product Development Source Material and Manufacturing Report	The Contractor shall submit a detailed spreadsheet regarding critical project materials that are sourced from a location other than the United States, sources, and manufacturing sites. This includes, but is not limited to:  (1) Physical locations of sources of raw and processed material by type of material; (2) location and nature of work performed at manufacturing site; and (3) location and nature of non-clinical and clinical study sites.	Due within 30 days of award date, and within 30 days after substantive changes are made to sources or materials. The Government will provide written comments to the Product Development Source Material and Manufacturing Report within 15 business days after submission.  If corrective action is recommended, Contractor must address and document all

			concerns raised by BARDA.
5	Weekly Teleconference	The Contractor shall participate in teleconferences every week with BARDA to discuss the performance of the contract. The Contractor shall provide slides 24 hours in advance of scheduled meetings.	Held weekly. Minutes provided by Contractor within 3 business days of the meeting.
6	Monthly Reports	The Contractor shall submit monthly reports summarizing data and progress to date on each aim in the SOW.	Due the 15 <sup>th</sup> of the month following the preceding reporting month. The COR and CO will review the monthly reports with the Contractor and provide feedback.
7	Daily Check-In with Project Staff for COVID-19 Response	<p>Upon request of the Government, the Contractor shall participate in a daily check-in updates with the project staff (via teleconference or email).</p> <p>The updates will address key cost, schedule and technical updates. Daily updates may be shared with senior Government leaders during the COVID-19 response and should be provided in both a non-confidential and confidential format.</p> <p>Daily check-ins may occur on weekdays, excluding federal holidays. Upon request of the Government, check-ins may also occur on weekends and on federal holidays, provided at least 8 hours' notice.</p>	<p>No agenda will be required for the check-in.</p> <p>No meeting minutes are required.</p> <p>Contractor will provide a bulleted email update as soon as possible following any check-in.</p>
8	Sample Prototype	If applicable and available, the Contractor shall deliver sample prototype/examples to BARDA DRIVE for display purposes ONLY. Prototype/examples are not intended for clinical or non-clinical uses.	If applicable and available, the prototype is due within 30 days of request
9	Draft Final Report & Final Report	These reports are to include a summation of the work performed and results obtained for the entire contract period of performance.	<p>Draft Report due 30 days prior to contract end date</p> <p>Final Report due on or before the completion date of the contract.</p>

10	Product/Technology Transition Strategy	The Contractor shall submit a 1-2 page summary document containing a Transition Strategy. The Transition Strategy should include a strategic business and technical plan for further development and transitioning the product and/or technology	Due 30 days prior to contract end date or 30 days prior to the end of each year of the Base Period, whichever occurs first.
11	Final Data Package	Contractor must submit a data package consisting of all raw data produced under this contract. Data may be used by BARDA DRIVE for analysis, evaluation, shared with other agencies, or shared outside of the government consistent with FAR 52.227-14. This submission package must be delivered in a non-proprietary format.  If clinical trial data is included, that data must be provided consistent with applicable privacy laws to protect personally identifiable information (PII).	Due at least 15 days prior to contract end date. Partial data-sets may also be requested for delivery prior to submission of the Final Data Submission Package.
12	Supplemental Technical Documents, Raw Data, or Data Analysis	The Contractor shall provide all raw data, data analysis, or a data report to BARDA DRIVE in accordance with FAR 52.227-14.	Due upon request from the CO or COR
13	Deliverables Arising from FDA Correspondence	See descriptions below for FDA Meetings, FDA Submissions & Correspondence, FDA Audits, and Other FDA Correspondence.	See due dates below for FDA Meetings, FDA Submissions & Correspondence, FDA Audits, and Other FDA Correspondence.

**a. Periodic Document Review**

The CO and COR reserve the right to request within the period of performance a non-proprietary technical document for distribution within the Government. Contractor shall provide the technical document within 10 business days of CO or COR request. Contractor can request additional time on an as-needed basis. If edits are recommended, the Contractor must address, in writing, concerns raised by the Government in writing.

**b. Deliverables Arising from FDA Correspondence**

**1) FDA Meetings**

- i. The Contractor shall forward the dates and times of any meeting with the FDA to BARDA and make arrangements for appropriate BARDA staff to attend the FDA meetings if requested by BARDA. BARDA may include up to a maximum of four people (COR, CO and up to 2 subject matter experts).
- ii. Contractor shall notify BARDA of upcoming FDA meetings within 24 hours of scheduling.



- iii. The Contractor shall forward initial Contractor and FDA-issued draft minutes and final minutes of any meeting with the FDA to the CO and COR within 5 business days of receipt. All documents shall be duly marked as either "Draft" or "Final."

## **2) FDA Submissions & Correspondence**

- i. The Contractor shall provide BARDA the opportunity to review and comment upon all documents submitted to the FDA. In addition, an electronic copy of the final FDA submissions will also need to be submitted. All documents shall be duly marked as either "Draft" or "Final."
  - 1. If draft documents are submitted to the COR for review, the COR will provide feedback to Contractor within 10 business days of receipt, or sooner as necessary to address FDA deadlines or requests.
  - 2. If BARDA reviews draft documents, the Contractor shall revise, as appropriate, their documents to address BARDA's concerns and/or recommendations prior to FDA submission.
  - 3. Final FDA submissions and all email correspondence with the FDA related to submissions shall be submitted to the CO and COR no later than 5 calendar days of their submission to, or email correspondence with, the FDA.

## **3) FDA Audits**

- i. In the event of an FDA inspection which occurs as a result of this contract and for the product, or for any other FDA inspection that has the reasonable potential to impact the performance of this contract, the Contractor shall provide the CO and COR with an exact copy (non-redacted) of the FDA Form 483 and the Establishment Inspection Report (EIR) within five (5) business days after the Contractor's receipt of those documents. The Contractor shall provide the COR and CO with copies of the plan for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines as identified in the audit report, status updates during the plan's execution and a copy of all final responses to the FDA. The Contractor shall also provide redacted copies of any FDA audits received from subcontractors that occur as a result of this contract or for this product. To the extent feasible, the Contractor shall make arrangements for BARDA representative(s) to be present during the final debrief by the regulatory inspector.
- ii. If draft documents are submitted to the COR for review, the COR will provide feedback to Contractor within 10 business days of receipt, or sooner as necessary to address FDA deadlines or requests.
- iii. If BARDA reviews draft documents, the Contractor shall revise as appropriate their documents to address BARDA's written concerns and/or recommendations prior to FDA submission.
  - 1. Contractor shall notify CO and COR within 10 business days of a scheduled FDA audit or within 24 hours of an ad hoc site visit/audit if the FDA does not provide 10 business days' advance notice.
  - 2. Contractor shall provide copies of any FDA audit report received from subcontractors that occur as a result of this contract or for this product within 5 business days of receiving correspondence from the FDA, Subcontractor, or third party.
  - 3. Within 15 business days of audit report, Contractor shall provide CO with a plan for addressing areas of nonconformance, if any are identified.

Final FDA submissions shall be submitted to the CO and COR.

#### **4) Other FDA Correspondence**

The Contractor shall document any material correspondence between Contractor and FDA as related to activities funded under this contract and submit to BARDA. All such documents shall be duly marked as either "Draft" or "Final." Contractor shall provide such written summary of any FDA correspondence or engagement within 5 business days and submit to the CO and COR. The written summary shall include:

- i. A tracking log of progress on regulatory submissions with the FDA, description of the submission, date of the submission, status of submission and next steps.

#### **c. Reporting and Meeting Details Specifics**

Monthly Progress Report:

This report shall include a description of the activities during the reporting period, and the activities planned for the ensuing reporting period. The first reporting period consists of the first full month of performance plus any fractional part of the initial month. Thereafter, the reporting period shall consist of each calendar month.

The Contractor shall submit a Monthly Progress Report on or before the 15<sup>th</sup> calendar day following the last day of each reporting period and shall include the following:

A cover page that includes the contract number and title; the type of report and period that it covers; the Contractor's name, address, telephone number, fax number, and e-mail address; and the date of submission;

SECTION I - An introduction covering the purpose and scope of the contract effort;

SECTION II – PROGRESS

SECTION II Part A: OVERALL PROGRESS - A description of overall progress;

SECTION II Part B: MANAGEMENT AND ADMINISTRATIVE UPDATE – A description of all meetings, conference calls, etc. that have taken place during the reporting period. Include progress on administration and management issues (e.g. evaluating and managing subcontractor performance and personnel changes);

SECTION II Part C: TECHNICAL PROGRESS - For each activity related to the Gantt chart, document the results of work completed. The report shall be in sufficient detail to explain comprehensively the results achieved. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the Contract. Include progress or status updates for all SOW tasks in each of the monthly technical progress reports for which there is activity ongoing in that SOW task area(s) as well as data for completed studies in any SOW task.

The report shall also include a description of problems encountered and proposed corrective action; differences between planned and actual progress, why the differences have occurred and what corrective actions are planned; preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the project;

SECTION II Part D: PROPOSED WORK - A summary of work proposed for the next reporting period and preprints/reprints of papers and abstracts, and a current/updated Gantt chart;

SECTION II Part E: Outstanding Issues/Anticipated Areas of Concern - a list of any existing contractual concerns that impact the technical scope of work, schedule, or pricing, as well as a list of potential or anticipated areas of concern that may be encountered in the future months. A Monthly Progress Report will not be required in the same month that the Annual or Final Reports are submitted;

#### Final Report(s) Requirement:

This report shall include a summation of the activities during the reporting period, and the activities planned for the ensuing reporting period. The first reporting period consists of the first full year of performance plus any fractional part of the initial year. Thereafter, the reporting period shall consist of each calendar year.

The report shall include a cover page that includes the contract number and title; the type of report and period that it covers; the Contractor's name, address, telephone number, fax number, and e-mail address; and the date of submission;

SECTION I-EXECUTIVE SUMMARY - A brief overview of the work completed and major accomplishments achieved during the reporting period;

#### SECTION II-PROGRESS

SECTION II Part A: OVERALL PROGRESS - A description of overall progress highlighting the significant accomplishments in the past year;

SECTION II Part B: MANAGEMENT AND ADMINISTRATIVE UPDATE – A description of all meetings, conference calls, etc. that have taken place during the reporting period. Include progress on administration and management issues (e.g. evaluating and managing subcontractor performance and personnel changes;

SECTION II Part C: TECHNICAL PROGRESS - For each activity, document the results of work completed during the period covered in relation to proposed progress, effort and budget. The report shall be in sufficient detail to explain comprehensively the results achieved. The description shall include pertinent data and/or graphs in sufficient detail to explain any significant results achieved and preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the Contract. The report shall include a description of problems encountered and proposed corrective action; differences between planned and actual progress, why the differences have occurred and what corrective actions are planned; preliminary conclusions resulting from analysis and scientific evaluation of data accumulated to date under the project. The report should summarize progress made under each SOW task.

#### Monthly Calls

A conference call between the COR and the Contractor's Project Leaders/delegates and designees shall occur monthly or as directed by the CO and COR. During this call the Contractor's Project Leaders/delegates and designees will discuss the activities since the last call, any problems that have arisen and the activities planned until the next call takes place. The Contractor's Project Leaders/delegates may choose to include other key personnel on the conference call to give detailed updates on specific projects as this may be requested by the COR.

#### Project Meetings

The Contractor shall participate in Project Meetings to coordinate the performance of the Contract, as requested by the COR. These meetings may include face-to-face meetings (kick-off meetings, project reviews, etc) with BARDA in Washington, D.C. and at work sites of the Contractor. Such meetings may include, but are not limited to, meetings of the Contractor to discuss study designs, site visits to the Contractor's facilities, and meetings with the Contractor and DHHS officials to discuss the technical, regulatory, and ethical aspects of the program. Subject to the data rights provisions in this Contract, the

Contractor will provide data, reports, and presentations to groups of outside experts and Government personnel as required by the CO and COR in order to facilitate review of contract activities.

Electronic copies of the conference call meeting minutes/summaries by the Contractor shall be provided via e-mail to the CO and COR by the Contractor within five (5) business days after the conference call is held. The COR will review these minutes for approval within 15 business days.

**d. Experimental Protocols**

Notwithstanding guidance found under Article H in this document related to clinical protocols, the Contractor shall submit all study/experiment/test plans, designs, and other protocols to BARDA for review and comment before proceeding with a study.

**F.3 SUBJECT INVENTION REPORTING REQUIREMENT**

All reports and documentation required by FAR Clause 52.227-11 Patent Rights-Ownership by the Contractor, including, but not limited to, the invention disclosure report, the confirmatory license, and the Government support certification, one copy of an annual utilization report, and a copy of the final invention statement, shall be submitted to the CO. A final invention statement (see FAR 27.303 (b)(2)(ii)) shall be submitted to the CO prior to the closeout of the Contract.

If no invention is disclosed or no activity has occurred on a previously disclosed invention during the applicable reporting period, a negative report shall be submitted to the CO at the address listed below.

**SECTION G – CONTRACT ADMINISTRATION DATA**

**G.1. CONTRACTING OFFICER**

The following CO will represent the Government for the purpose of this Contract:

Matthew A. McCord  
Contracting Officer  
HHS/ASPR/AMCG  
O'Neill House Office Building  
Washington, DC 20515  
[matthew.mccord@hhs.gov](mailto:matthew.mccord@hhs.gov)

- 1) The CO is the only individual who can legally commit the Government to the expenditure of public funds. No person other than the CO can make any changes to the terms, conditions, general provisions, or other stipulations of this Contract.
- 2) The CO is the only person with the authority to act as agent of the Government under this contract. Only the CO has authority to (1) direct or negotiate any changes in the Statement of Work; (2) modify or extend the period of performance; (3) change the delivery schedule; (4) authorize reimbursement to the Contractor of any costs incurred during the performance of this Contract; (5) otherwise change any terms and conditions of this Contract.
- 3) No information other than that which may be contained in an authorized modification to this Contract, duly issued by the CO, which may be received from any person employed by the Government, other otherwise, shall be considered grounds for deviation from any stipulation of this Contract.
- 4) The Government may unilaterally change its CO designation, after which it will notify the Contractor in writing of such change.

**G.2. CONTRACTING OFFICER'S REPRESENTATIVE (COR)**

The following COR will represent the Government for the purpose of this contract:

Rebekka Lueptow  
Contracting Officer's Representative  
HHS/ASPR/BARDA  
O'Neill House Office Building  
Washington, DC 20515  
[Rebekka.Lueptow@hhs.gov](mailto:Rebekka.Lueptow@hhs.gov)

The COR is responsible for:

- 1) Monitoring the Contractor's technical progress, including the surveillance and assessment of performance and recommending to the CO changes in requirements;
- 2) Assisting the CO in interpreting the Statement of Work and any other technical performance requirements;
- 3) Performing technical evaluation as required;
- 4) Performing technical inspections and acceptances required by this Contract; and
- 5) Assisting in the resolution of technical problems encountered during performance. The Government may unilaterally change its COR designation, after which it will notify Contractor in writing of such change.

### **G.3. KEY PERSONNEL**

Pursuant to the Key Personnel clause incorporated in Section I of this Contract, the following individuals are considered to be essential to the work being performed hereunder:

<b>Name</b>	<b>Title</b>
Savita Nikam, PhD	Director of Research

The key personnel specified in this Contract are considered to be essential to work performance. At least 30 days prior to diverting any of the specified individuals to other programs or contracts (or as soon as possible, if an individual must be replaced, for example, as a result of leaving the employ of the Contractor), the Contractor shall notify the CO and shall submit comprehensive justification for the diversion or replacement request (including proposed substitutions for key personnel) and qualifications (CV, etc) of the individual proposed as a substitute to permit evaluation by the Government of the impact on performance under this contract. The Contractor shall not divert or otherwise replace any key personnel without the written consent of the CO. The Government may modify the contract to add or delete key personnel at the request of the contractor or Government.

### **G.4. INVOICING**

- a. Invoices (see Attachment 2) will be submitted for each deliverable in accordance with Attachment 3. In the event that a deliverable is not submitted or not deemed acceptable for approval by the COR and CO, the CO reserves the right to not process the invoice and payment until an acceptable deliverable has been submitted and approved by the COR and CO.
- b. Unless otherwise stated in the instructions for completing this form, all columns A through H, shall be completed for each report submitted.
- c. The first financial report shall cover the period consisting of the first full three calendar months following the date of the Contract, in addition to any fractional part of the initial month. Thereafter, reports will be on a quarterly basis.
- d. The CO may require the Contractor to submit detailed support for costs contained in one or more interim financial reports. This clause does not supersede the record retention requirements in FAR Part 4.7.
- e. The listing of expenditure categories to be reported is incorporated as a part of this Contract and can be found at Attachment 2.

- f. Invoices must include the cumulative total expenses to date, adjusted (as applicable) to show any amounts suspended by the Government.
- g. Contractor invoices/financial reports shall conform to the form, format, and content requirements of the instructions for Attachment 2, and be sent electronically to the following points of contact\*. Additionally, the Contractor may be required to submit to a DRIVE specific invoice tracking system as will be directed by the CO.

CO	COR	PSC
Matthew A. McCord Contracting Officer <a href="mailto:matthew.mccord@hhs.gov">matthew.mccord@hhs.gov</a>	Rebekka Lueptow Contracting Officer's Representative <a href="mailto:Rebekka.Lueptow@hhs.gov">Rebekka.Lueptow@hhs.gov</a>	<a href="mailto:PSC_Invoices@psc.hhs.gov">PSC_Invoices@psc.hhs.gov</a>

- h. An electronic copy of the payment request shall be uploaded into the designated digital repository (DRIVE Digital Resources) and an e-mail notification of the upload will be provided to the CO and COR.

\* All invoice submissions shall be in accordance with FAR Clause 52.232-25, Prompt Payment (Oct 2008)

## **G.5. POST AWARD EVALUATION OF CONTRACTOR PERFORMANCE**

### **Contractor Performance Evaluations**

Interim and final evaluations of Contractor performance will be prepared on this Contract in accordance with FAR Subpart 42.15. The final performance evaluation will be prepared at the time of completion of work. In addition to the final evaluation, an interim evaluation shall be submitted annually.

Interim and final evaluations will be provided to the Contractor as soon as practicable after completion of the evaluation. The Contractor will be permitted thirty days to review the document and to submit additional information or a rebutting statement. If agreement cannot be reached between the parties, the matter will be referred to an individual one level above the CO. Should Contractor choose to do so, it may challenge that individual's decision in accordance with FAR 52.233-1, incorporated herein by Section I.

Copies of the evaluations, Contractor responses, and review comments, if any, will be retained as part of the contract file, and may be used to support future award decisions.

### **Electronic Access to Contractor Performance Evaluations**

Contractors that have Internet capability may access evaluations through a secure Web site for review and comment by completing the registration form that can be obtained at the following address:

<http://www.cpars.csd.disa.mil/cparsmain.htm>

The registration process requires the Contractor to identify an individual that will serve as a primary contact and who will be authorized access to the evaluation for review and comment. In addition, the Contractor will be required to identify an alternate contact that will be responsible for notifying the cognizant contracting official in the event the primary contact is unavailable to process the evaluation within the required 30-day time frame.

## **G.6. CONTRACT COMMUNICATIONS/CORRESPONDENCE (JULY 1999)**

The Contractor shall identify all correspondence, reports, and other data pertinent to this Contract by imprinting the contract number from Page 1 of the Contract.

## **G.7. GOVERNMENT PROPERTY**

Contractor retains title to all property acquired as necessary to execute the work under this contract.

## **SECTION H – SPECIAL CONTRACT REQUIREMENTS**

### **H.1 REPORTING MATTERS INVOLVING FRAUD, WASTE AND ABUSE**

Anyone who becomes aware of the existence or apparent existence of fraud, waste and abuse in BARDA funded programs should report such matters to the DHHS Inspector General's Office in writing or on the Inspector General's Hotline. The toll free number is 1-800-HHS-TIPS (1-800- 447-8477). All telephone calls will be handled confidentially. The e-mail address is [Htips@os.dhhs.gov](mailto:Htips@os.dhhs.gov) and the mailing address is:

Office of Inspector General  
Department of Health and Human Services TIPS  
HOTLINE  
P.O. Box 23489 Washington, D.C. 20026

### **H.2 PROHIBITION ON CONTRACTOR INVOLVEMENT WITH TERRORIST ACTIVITIES**

The Contractor acknowledges that U.S. Executive Orders and Laws, including but not limited to 13224 and P.L. 107-56, prohibit transactions with, and the provision of resources and support to, individuals and organizations associated with terrorism. It is the legal responsibility of the Contractor to ensure compliance with these Executive Orders and Laws. This clause must be included in all subcontracts issued under this Contract.

### **H.3 IDENTIFICATION AND DISPOSITION OF DATA**

The Contractor will be required to provide certain data generated under this Contract to DHHS. DHHS reserves the right to review any other data related to performance of this Contract.

The Contractor shall keep copies of all data required by the FDA relevant to this Contract for the time specified by the FDA.

### **H.4 EXPORT CONTROL NOTIFICATION**

Contractors are responsible for ensuring compliance with all export control laws and regulations that may be applicable to the export of and foreign access to their proposed technologies. Contractors may consult with the Department of State with any questions regarding the International Traffic in Arms Regulation (ITAR) (22 C.F.R. Parts 120-130) and /or the Department of Commerce regarding the Export Administration Regulations (15 C.F.R. Parts 730-774).

### **H.5 CONFLICT OF INTEREST**

The Contractor represents and warrants that, to the best of the Contractor's knowledge and belief, there are no relevant facts or circumstances which could give rise to an organizational conflict of interest, as defined in FAR 2.101 and Subpart 9.5, or that the Contractor has disclosed all such relevant information. Prior to commencement of any work, the Contractor agrees to notify the CO promptly that, to the best of its knowledge and belief, no actual or potential conflict of interest exists or to identify to the CO any actual or potential conflict of interest the firm may have. In emergency situations, however, work may begin but notification shall be made within five (5) working days. The Contractor agrees that if an actual or potential organizational conflict of interest is identified during performance, the Contractor shall promptly make a full disclosure in writing to the CO. This disclosure shall include a description of actions which the Contractor has taken or proposes to take, after consultation with

the CO, to avoid, mitigate, or neutralize the actual or potential conflict of interest. The Contractor shall continue performance until notified by the CO of any contrary action to be taken. Remedies include termination of this Contract for convenience, in whole or in part, if the CO deems such termination necessary to avoid an organizational conflict of interest. If the Contractor was aware of a potential organizational conflict of interest prior to award or discovered an actual or potential conflict after award and did not disclose it or misrepresented relevant information to the CO, the Government may terminate the Contract for default, debar the Contractor from Government contracting, or pursue such other remedies as may be permitted by law or this Contract.

## **H.6 INSTITUTIONAL RESPONSIBILITY REGARDING INVESTIGATOR FINANCIAL CONFLICTS OF INTEREST**

The Contractor shall comply with the requirements of 45 C.F.R. Part 94, Responsible Prospective Contractors, which promotes objectivity in research by establishing standards to ensure that investigators (defined as the principal investigator and any other person who is responsible for the design, conduct, or reporting of research funded under BARDA contracts) will not be biased by any conflicting financial interest.

As required by 45 C.F.R. Part 94, the Contractor shall, at a minimum:

a. Maintain a written, enforceable policy on conflict of interest that complies with 45 C.F.R. Part 94 and inform each investigator of the policy, the investigator's reporting responsibilities, and the applicable regulations. The Contractor must take reasonable steps to ensure that investigators working as collaborators or subcontractors comply with the regulations.

b. Designate an official(s) to solicit and review financial disclosure statements from each investigator participating in BARDA-funded research. Based on established guidelines consistent with the regulations, the designated official(s) must determine whether a conflict of interest exists, and if so, determine what actions should be taken to manage, reduce, or eliminate such conflict. A conflict of interest exists when the designated official(s) reasonably determines that a *Significant Financial Interest* could directly and significantly affect the design, conduct, or reporting of the BARDA-funded research. The Contractor may require the management of other conflicting financial interests in addition to those described in this paragraph, as it deems appropriate. Examples of conditions or restrictions that might be imposed to manage actual or potential conflicts of interests are included in 45 C.F.R. Part 94, under Management of Conflicting Interests.

c. Require all financial disclosures to be updated during the period of the award, either on an annual basis or as new reportable Significant Financial Interests are obtained.

d. Maintain records, identifiable to each award, of all financial disclosures and all actions taken by the Contractor with respect to each conflicting interest 3 years after final payment or, where applicable, for the other time periods specified in 48 C.F.R. Part 4, subpart 4.7, Contract Records Retention.

e. Establish adequate enforcement mechanisms and provide for sanctions where appropriate.

If a conflict of interest is identified, the Contractor shall report to the CO, the existence of the conflicting interest found. This report shall be made and the conflicting interest managed, reduced, or eliminated, at least on a temporary basis, within sixty (60) days of that identification.

If the failure of an investigator to comply with the conflict of interest policy has biased the design, conduct, or reporting of the BARDA-funded research, the Contractor must promptly notify the CO of the corrective action taken or to be taken. The CO will take appropriate action or refer the matter to the Contractor for further action, which may include directions to the Contractor on how to maintain appropriate objectivity in the funded research.

The CO may at any time inquire into the Contractor's procedures and actions regarding conflicts of interests in BARDA-funded research, including a review of all records pertinent to compliance with 45 C.F.R. Part 94. The CO may require submission of the records or review them on site. On the basis of this review, the CO may decide that a particular conflict of interest will bias the objectivity of the BARDA-funded research to such an extent that further corrective action is needed or that the Contractor has not managed, reduced, or eliminated the conflict of interest. The issuance of a Stop Work Order by the CO may be necessary until the matter is resolved.



If the CO determines that BARDA-funded clinical research, whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, has been designed, conducted, or reported by an investigator with a conflict of interest that was not disclosed or managed, the Contractor must require disclosure of the conflict of interest in each public presentation of the results of the research.

#### **H.7 NEEDLE DISTRIBUTION**

The Contractor shall not use contract funds to carry out any program of distributing sterile needles or syringes for the hypodermic injection of any illegal drug.

#### **H.8 DISSEMINATION OF FALSE OR DELIBERATELY MISLEADING INFORMATION**

The Contractor shall not use contract funds to disseminate information that is deliberately false or misleading.

#### **H.9 CONFIDENTIALITY OF INFORMATION**

- a. Confidential information, as used in this article, means information or data of a personal nature about an individual, or proprietary information or data submitted by or pertaining to an institution or organization.
- b. The CO and the Contractor may, by mutual consent, identify elsewhere in this Contract specific information and/or categories of information which the Government will furnish to the Contractor or that the Contractor is expected to generate which is confidential and providing further that the Government is not entitled to unlimited rights to that information pursuant to FAR 52.227-14. Similarly, the CO and the Contractor may, by mutual consent, identify such confidential information from time to time during the performance of the contract. Failure to agree will be settled pursuant to the "Disputes" clause.
- c. If it is established elsewhere in this Contract that information to be utilized under this Contract, or a portion thereof, is subject to the Privacy Act, the Contractor will follow the rules and procedures of disclosure set forth in the Privacy Act of 1974, 5 U.S.C. 552a, and implementing regulations and policies, with respect to systems of records determined to be subject to the Privacy Act.
- d. Confidential information, as defined in paragraph (a) of this article, shall not be disclosed without the prior written consent of the individual, institution, or organization.
- e. Whenever the Contractor is uncertain with regard to the proper handling of material under the Contract, or if the material in question is subject to the Privacy Act or is confidential information subject to the provisions of this article, the Contractor should obtain a written determination from the CO prior to any release, disclosure, dissemination, or publication.
- f. The provisions of paragraph (d) of this article shall not apply to conflicting or overlapping provisions in other Federal, State or local laws.

#### **H.10 ACCESS TO DOCUMENTATION/DATA**

The Government shall have physical and electronic access to all documentation and data generated under this Contract, including: all data documenting Contractor performance; all data generated; all communications and correspondence with regulatory agencies and bodies to include all audit observations, inspection reports, milestone completion documents, and all Offeror commitments and responses. Contractor shall provide the Government with an electronic copy of all correspondence and submissions to the FDA within 5 business days of receipt. The Government shall acquire unlimited rights to all data funded under this contract in accordance with FAR Subpart 27.4 and FAR Clause 52.227-14.

#### **H.11 [Reserved]**

## **H.12 ACKNOWLEDGMENT OF FEDERAL FUNDING**

Section 507 of P.L. 104-208 mandates that Contractors funded with Federal dollars, in whole or in part, acknowledge Federal funding when issuing statements, press releases, requests for proposals, bid solicitations and other documents. This requirement is in addition to the continuing requirement to provide an acknowledgment of support and disclaimer on any publication reporting the results of a contract funded activity.

### **Publication and Publicity**

No information related to data obtained under this Contract shall be released or publicized without providing BARDA with at least thirty (30) days advanced notice and an opportunity to review the proposed release or publication.

In addition to the requirements set forth in this Contract, Section 507 of P.L. 104-208 mandates that Contractors funded with Federal dollars, in whole or in part, acknowledge Federal funding when issuing statements, press releases, requests for proposals, bid solicitations and other documents. Contractors are required to state:

- (1) The percentage and dollar amounts of the total program or project costs financed with Federal money and;
- (2) The percentage and dollar amount of the total costs financed by non-governmental sources. For purposes of this Contract "publication" is defined as an issue of printed material offered for distribution or any communication or oral presentation of information, including any manuscript or scientific meeting abstract. Any publication containing data generated under this Contract must be submitted for BARDA review no less than thirty (30) calendar days for manuscripts and fifteen (15) calendar days for abstracts before submission for public presentation or publication. Contract support shall be acknowledged in all such publications substantially as follows:

"This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, under Contract No. \_\_\_\_\_."

### **Press Releases**

Misrepresenting contract results or releasing information that is injurious to the integrity of BARDA may be construed as improper conduct. Press releases shall be considered to include the public release of information to any medium, excluding peer-reviewed scientific publications. With the exception of ad-hoc press releases required by applicable law or regulations, the Contractor shall ensure that the COR has received an advance copy of any press release related to the contract not less than two (2) business days prior to the issuance of the press release.

The Contractor shall acknowledge the support of the Department of Health and Human Service, Office of the Assistant Secretary for Preparedness and Response, Biomedical Advanced Research and Development Authority, whenever publicizing the work under this contract in any media by including an acknowledgment substantially as follows:

"This project has been funded in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response; Biomedical Advanced Research and Development Authority, Division of Research Innovation and Ventures under Contract No. \_\_\_\_\_."

#### **a. Contractor Use of the Powered by DRIVE Logo**

- 1) For the limited purposes of the Contractor's participation related to the subject DRIVE contract, Contractor is permitted to use the following logo (the "Logo") for the period of performance of this Contract (or for a longer period, if agreed between the parties), subject to the Contractor's full performance of the terms and conditions of the subject Contract and provided that Contractor shall cease to use the Logo immediately upon BARDA's

request.



- 2) The Contractor's use of the term "Powered by DRIVE" shall be subject to DRIVE Brand Guidelines.
- 3) Any other use of the DRIVE name, its Logo, service marks or trademarks, or any of its other distinguishable marks, whether registered or not, shall be limited to those granted by the express, written permission of the BARDA. Those to whom such permission is granted must agree that BARDA shall remain the final arbiter of the use of the mark or Logo.

b. BARDA Use of Contractor Logo

Contractor hereby grants BARDA/DRIVE the right to use Contractor's corporate logo (and other artwork as agreed to by the parties), for presentations, internal and external websites, and other reasonable promotional and reporting uses relating to the project during the period of performance of the Contract (or for a longer period, if agreed between the parties).

#### **H.13 [Reserved]**

#### **H.14 PRIVACY ACT APPLICABILITY**

Notification is hereby given that the Contractor and its employees are subject to criminal penalties for violation of the Privacy Act to the same extent as employees of the Government. The Contractor shall assure that each of its employees knows the prescribed rules of conduct and that each is aware that he or she can be subjected to criminal penalty for violation of the Act. A copy of 45 C.F.R. Part 5b, Privacy Act Regulations, may be obtained at <https://www.gpo.gov/fdsys/granule/CFR-2007-title45-vol1/CFR-2007-title45-vol1-part5b>.

The Contractor is responsible for monitoring contractor compliance with the Privacy Act.

The Contractor shall follow the Privacy Act guidance as contained in the Privacy Act System of Records number 09-25-0200.

#### **H.15 LABORATORY LICENSE REQUIREMENTS**

The Contractor shall comply with all applicable requirements of Section 353 of the Public Health Service Act (Clinical Laboratory Improvement Act as amended) (42 U.S.C. 263a) and 42 CFR Part 493. This requirement shall also be included in any subcontract for services under the Contract.

#### **H.16 QUALITY ASSURANCE (QA) AUDIT REPORTS**

BARDA reserves the right to participate in QA audits as related to activities funded under this Contract. Upon completion of the audit/site visit the Contractor shall provide a report capturing the findings, results and next steps in proceeding with the subcontractor. If action is requested of the subcontractor, detailed concerns for addressing areas of non-conformance to FDA regulations for GLP, GMP, or GCP guidelines, as identified in the audit report, must be provided to BARDA. The Contractor shall provide responses from the subcontractors to address these concerns and plans for corrective action execution.

- Contractor shall notify CO and COR of upcoming, ongoing, or recent audits/site visits of subcontractors as part of weekly communications.
- Contractor shall notify the COR and CO within five (5) business days of report completion.

#### **H.17 BARDA AUDITS**

Contractor shall accommodate periodic or reasonable ad hoc site visits during normal business hours by the Government with forty-eight (48) hours advance notice. If the Government, the Contractor, or other parties identifies any issues during an audit, the Contractor shall capture the issues, identify potential solutions, and provide a report to the Government.

- If issues are identified during the audit, Contractor shall submit a report to the CO and COR detailing the finding and corrective action(s) within 10 business days of the audit.
- COR and CO will review the report and provide a response to the Contractor with ten (10) business days.
- Once corrective action is completed, the Contractor will provide a final report to the CO and COR.

#### **H.18 RESTRICTION ON EMPLOYMENT OF UNAUTHORIZED ALIEN WORKERS**

The Contractor shall not use Contract funds to employ workers described in Section 274A (h)(3) of the Immigration and National Act, which reads as follows:

“(3) Definition of unauthorized alien – As used in this Section, the term ‘unauthorized alien’ with respect to the employment of an alien at a particular time, that the alien is not at that time either an alien lawfully admitted for permanent residence, or (B) authorized to be so employed by this Act or by the Attorney General.”

#### **H.19 NOTIFICATION OF CRITICAL PROGRAMMATIC CONCERNS, RISKS, OR POTENTIAL RISKS**

If any action occurs that creates a cause for critical programmatic concern, risk, or potential risk to BARDA or the Contractor an Incident Report shall be delivered to BARDA.

- Within 48 hours of activity or incident or within 24 hours for a security related activity or incident, Contractor must notify BARDA.
- Additional updates due to COR and CO within 48 hours of additional developments.
- Contractor shall submit within 5 business days a Corrective Action Plan (if deemed necessary by either party) to address any potential issues.

If corrective action is deemed necessary, Contractor must address in writing its consideration of concerns raised by BARDA within 5 business days of receiving comments by BARDA.

#### **H.20 [Reserved]**

#### **H.21 DISSEMINATION OF INFORMATION (May 2004)**

Other than scientific and technical data for which the Contractor can assert a copyright under FAR Clause 52.227-14 (c), no information related to data obtained under this Contract shall be released or publicized without the prior written consent of the CO. In the event that the Contractor seeks to publicize scientific and technical data, the contractor shall provide BARDA, through the COR, with a minimum of thirty (30) business days to review the particular scientific and technical data prior to publication.

#### **H.22 REGISTRATION WITH THE SELECT AGENT PROGRAM FOR WORK INVOLVING THE POSSESSION, USE, AND/OR TRANSFER OF SELECT BIOLOGICAL AGENTS OR TOXINS**

Work involving select biological agents or toxins shall not be conducted under this Contract until the Contractor and any affected subcontractor(s) are granted a certificate of registration or are authorized to work with the applicable select agents.

For prime or subcontract awards to domestic institutions who possess, use, and/or transfer Select Agents under this contract, the institution must complete registration with the Centers for Disease Control and Prevention (CDC), DHHS or the Animal and Plant Health Inspection Services (APHIS), U.S. Department of Agriculture (USDA), as applicable, before performing work involving Select Agents, in accordance with 42 C.F.R. Part 73. No Government funds can be used for work involving Select Agents, as defined in 42 C.F.R. Part 73, if the final registration certificate is denied.

For prime or subcontract awards to foreign institutions who possess, use, and/or transfer Select Agents under this Contract, the institution must provide information satisfactory to the Government that a process equivalent to that described in 42 C.F.R. Part 73 (<http://www.cdc.gov/od/sap/docs/42cfr73.pdf>) for U.S. institutions is in place and will be administered on behalf of all Select Agent work sponsored by these funds before using these funds for any work directly involving the Select Agents. The Contractor must provide information addressing the following key elements appropriate for the foreign institution: safety, security, training, procedures for ensuring that only approved/appropriate individuals have access to the Select Agents, and any applicable laws, regulations and policies equivalent to 42 C.F.R. Part 73. The Government will assess the policies and procedures for comparability to the U.S. requirements described in 42 C.F.R. Part 73. When requested by the CO, the Contractor shall provide key information delineating any laws, regulations, policies, and procedures applicable to the foreign institution for the safe and secure possession, use, and transfer of Select Agents. This includes summaries of safety, security, and training plans, and applicable laws, regulations, and policies. For the purpose of security risk assessments, the Contractor must provide the names of all individuals at the foreign institution who will have access to the Select Agents and procedures for ensuring that only approved and appropriate individuals have access to Select Agents under the Contract.

Listings of HHS select agents and toxins, biologic agents and toxins, and overlap agents or toxins as well as information about the registration process, can be obtained on the Select Agent Program Web site at <https://www.selectagents.gov/>

## **H.23 MANUFACTURING STANDARDS**

The Good Manufacturing Practice Regulations (GMP) (21 C.F.R. Part 820) will be the standard to be applied for manufacturing, processing, packaging, storage and delivery of this product.

If at any time during the life of the Contract, the Contractor fails to comply with GMP in the manufacturing, processing, packaging, storage, stability and other testing of the manufactured drug substance or product and delivery of this product and such failure results in a material adverse effect on the safety, purity or potency of the product (a material failure) as identified by the FDA, the Contractor shall have thirty (30) calendar days from the time such material failure is identified to cure such material failure. If, within the thirty (30) calendar day period, the Contractor fails to take such an action to the satisfaction of the Government Project Officer/COR, or fails to provide a remediation plan that is acceptable to the COR, then the Contract may be terminated.

## **H.24 LABORATORY LICENSE REQUIREMENTS**

The Contractor shall comply with all applicable requirements of 21 C.F.R. Part 58 and FDA Medical Device GMP Guidance. This requirement shall also be included in any subcontract for services under the Contract.

## **H.25 SHARING RESEARCH DATA**

The Contractor's data sharing plan, due date to be determined at contract award, is hereby incorporated by reference. The Contractor agrees to adhere to its plan and shall request prior approval of the CO for any changes in its plan.

BARDA endorses the sharing of final research data to serve health. This contract is expected to generate research data that must be shared with the public and other researchers.

BARDA recognizes that data sharing may be complicated or limited, in some cases, by institutional policies, local IRB rules, as well as local, state and Federal laws and regulations, including the Privacy Rule (see HHS-published documentation on the Health Information Privacy at <http://www.hhs.gov/ocr/privacy/index.html>). The rights and privacy of people who participate in BARDA-funded research must be protected at all times; thus, data intended for broader use should be free of identifiers that would permit linkages to individual research participants and variables that could lead to deductive disclosure of the identity of individual subjects.

## **H.26 PUBLIC ACCESS TO ARCHIVED PUBLICATIONS RESULTING FROM ASSISTANT SECRETARY FOR PREPAREDNESS AND RESPONSE (ASPR) FUNDED RESEARCH**

All ASPR-funded investigators shall submit to the National Institutes of Health (NIH) National Library of Medicine's (NLM) PubMed Central (PMC) an electronic version of the author's final manuscript, upon acceptance for publication, of any peer-reviewed scientific publications resulting from research supported in whole or in part with Federal funds from the Department of Health and Human Services; Office of the Assistant Secretary for Preparedness and Response. ASPR defines the author's final manuscript as the final version accepted for journal publication, and includes all modifications from the publishing peer review process. The PMC archive will preserve permanently these manuscripts for use by the public, health care providers, educators, scientists, and ASPR. The Policy directs electronic submissions to the NIH/NLM/PMC: <http://www.pubmedcentral.nih.gov>.

## **H.27 [Reserved]**

## **H.28 [Reserved]**

## **H.29 CLINICAL TERMS OF AWARD**

In addition to those terms and conditions outlined under applicable HHSAR clauses incorporated by reference by Section I of this Contract, the following clinical terms of award detail an agreement between the BARDA and the Contractor; they apply to all contracts involving clinical research.

Draft protocols for each clinical study will be submitted to BARDA for evaluation and comment. BARDA comments will be addressed and/or incorporated into the draft protocol prior to submission to the FDA for comment, if required and as appropriate.

BARDA shall have unlimited rights to all protocols, data generated from the execution of these protocols, and final reports, funded by BARDA under this Contract, as defined in Rights in Data Clause in FAR 52.227-14. BARDA reserves the right to request that the Contractor provide any contract deliverable in a non-proprietary form without any restrictive legends to ensure BARDA has the ability to review and distribute the deliverables, as BARDA deems necessary.

Important information regarding performing human subject research is available here and should be addressed by the contractor. <https://www.hhs.gov/ohrp/>

Any updates to clinical studies (enrollment, technical results, etc) are to be addressed in the Monthly and Annual Progress Reports, as well as technical monthly calls. The Contractor shall advise the COR or designee in writing and via electronic communication in a timely manner of any issues potentially affecting contract performance.

### *i. Safety and Monitoring Issues*

#### **a. Institutional Review Board or Independent Ethics Committee Approval**

Before award and then with the annual progress report, the Contractor must submit to BARDA a copy of the current IRB-or IEC-approved informed consent document, documentation of continuing review and approval and the OHRP federal wide assurance number for the institution or site.

If other institutions are involved in the research (e.g., a multicenter clinical trial or study), each institution's IRB or IEC must review and approve the protocol. They must also provide BARDA initial and annual documentation of continuing review and approval, including the current approved informed consent document and federal wide number.

The Contractor must ensure that the application as well as all protocols are reviewed by their IRB or IEC.

To help ensure the safety of participants enrolled in BARDA-funded studies, the Contractor must provide BARDA copies of documents related to all major changes in the status of ongoing protocols, including the following:

- All amendments or changes to the protocol, identified by protocol version number, date, or both and dates it is valid.
- All changes in informed consent documents, identified by version number, dates, or both and dates it is valid.
- Termination or temporary suspension of patient accrual.
- Termination or temporary suspension of the protocol.
- Any change in IRB approval.
- Any other problems or issues that could affect the participants in the studies.

The Contractor must notify BARDA through the COR or CO of any of the above changes within five (5) working days by email or fax, followed by a letter signed by the institutional business official, detailing notification of the change of status to the local IRB and a copy of any responses from the IRB or IEC.

If a clinical protocol has been reviewed by an institutional biosafety committee (IBC) or the NIH Recombinant DNA Advisory Committee (RAC), the Contractor must provide information about the initial and ongoing review and approval, if any. See the NIH Guidelines for Research Involving Recombinant DNA Molecules.

#### **b. Data and Safety Monitoring Requirements**

BARDA strongly recommends independent safety monitoring for clinical trials of investigational drugs, devices, or biologics; clinical trial of licensed products; and clinical research of any type involving more than minimal risk to volunteers. Independent monitoring can take a variety of forms. Phase III clinical trials must be reviewed by an independent data and safety monitoring board (DSMB); other trials may require DSMB oversight as well. The Contractor shall inform BARDA of any upcoming site visits and/or audits of CRO facilities funded under this effort. BARDA reserves the right to accompany the Contractor on site visits and/or audits of CROs as BARDA deems necessary. The Contractor shall inform BARDA 30 days in advance of a DSMB board meetings for studies funded under this effort. BARDA reserves the right to participate in the DSMB board meetings on an impromptu basis as a non-voting member, if feasible per the structure of the study. If not, the communications from the DSMB to the Contractor should be made available to BARDA upon receipt.

A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. For examples, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as part of a routine physical examination (45 C.F.R. § 46.102(j)).

Final decisions regarding the type of monitoring to be used must be made by the Contractor, based on FDA and BARDA guidance, before enrollment starts. Discussions with the responsible BARDA PO/COR regarding appropriate safety monitoring must take place, and the Contractor must submit a written response to all concerns raised by BARDA, before patient enrollment begins and may include discussions about the appointment of one of the following:

**Independent Safety Monitor** – a physician or other appropriate expert who is independent of the study and available in real time to review and recommend appropriate action regarding adverse events and other safety issues.

**Independent Monitoring Committee (IMC) or Safety Monitoring Committee (SMC)** – a small group of independent investigators and biostatisticians who review data from a particular study.

**Data and Safety Monitoring Board** – an independent committee charged with reviewing safety and trial progress and providing advice with respect to study continuation, modification, and termination. The Contractor may use an established BARDA DSMB or to organize an independent DSMB. All phase III clinical trials must be reviewed by a DSMB; other trials may require DSMB oversight as well. Please refer to: NIAID Principles for Use of a Data and Safety Monitoring Board (DSMB) For Oversight of Clinical Trials Policy. BARDA should be provided documentation from DSMB and should be provided with any decisions by Contractor regarding the DMSB as it relates to work under this contract.

When a monitor or monitoring board is organized, a description of it, its charter or operating procedures (including a proposed meeting schedule and plan for review of adverse events), and roster and curriculum vitae from all members must be submitted to BARDA before enrollment starts. If concerns are raised, Contractor must address all concerns to BARDA, in writing, before enrollment begins. The Contractor will also ensure that the monitors and board members report any conflicts of interest and the Contractor will maintain a record of this. The Contractor will share conflict of interest reports with BARDA.

Additionally, the Contractor must submit written summaries of all reviews conducted by the monitoring group to the BARDA within thirty (30) days of reviews or meetings.

*ii. BARDA Protocol Review Process Before Patient Enrollment Begins*

BARDA has a responsibility to ensure that mechanisms and procedures are in place to protect the safety of participants in BARDA-supported clinical trials. Therefore, before patient accrual or participant enrollment, the Contractor must ensure the following (as applicable) are in place at each participating institution, prior to patient accrual or enrollment:

- IRB- or IEC-approved clinical research protocol identified by version number, date, or both, including details of study design, proposed interventions, patient eligibility, and exclusion criteria.
- Documentation of IRB or IEC approval, including OHRP federal wide number, IRB or IEC registration number, and IRB and IEC name.
- IRB- or IEC- approved informed consent form/document, identified by version number, date, or both and dates it is valid.
- Plans for the management of side effects.
- Procedures for assessing and reporting adverse events.
- Plans for data and safety monitoring (see above) and monitoring of the clinical study site, pharmacy, and laboratory.
- Documentation that the Contractor and all study staff responsible for the design or conduct of the research have received training in the protection of human subjects.

Documentation to demonstrate that each of the above items are in place shall be submitted to BARDA) for evaluation and comment in conjunction with the protocol. Execution of clinical studies requires written authorization from BARDA in accordance with this section of this contract.



*iii. Investigational New Drug or Investigational Device Exemption Requirements*

Consistent with federal regulations, applicable clinical research projects involving the use of investigational therapeutics, vaccines, or other medical interventions (including licensed products and devices for a purpose other than that for which they were licensed) in humans under a research protocol must be performed under a FDA investigational new drug (IND) or investigational device exemption (IDE).

Where an IND and IDE is otherwise required, exceptions must be granted in writing by FDA. If the proposed clinical trial will be performed under an IND or IDE, the Contractor must provide BARDA with the name and institution of the IND or IDE sponsor, the date the IND or IDE was filed with FDA, the FDA IND or IDE number, any written comments from FDA, and the written responses to those comments.

In instances in which an IND or IDE is required, unless FDA notifies Contractor otherwise, the Contractor must wait thirty (30) calendar days from FDA receipt of an initial IND or IDE application before initiating a clinical trial.

The Contractor must notify BARDA if the FDA places the study on clinical hold and provide BARDA any written comments from FDA, written responses to the comments, and documentation in writing that the hold has been lifted.

The Contractor must not use grant or contract funds during a clinical hold to fund clinical studies that are on hold other than costs that are associated with activities related to patients coming off study, monitoring, or ending the study. The Contractor must not enter into any new financial obligations related to clinical activities for the clinical trial on clinical hold.

*iv. Required Time-Sensitive Notification*

- a. Under an IND or IDE, the sponsor must provide FDA safety reports of serious adverse events. Under these Clinical Terms of Award, the Contractor must submit copies to the responsible BARDA representative or the COR as follows:
  - Expedited safety report of unexpected or life-threatening experience or death. A copy of any report of unexpected or life-threatening experience or death associated with the use of an IND drug, which must be reported to FDA by telephone or fax as soon as possible but no later than seven (7) days after the IND sponsor's receipt of the information, must be submitted to BARDA representative or COR within 24 hours of FDA notification.
  - Expedited safety reports of serious and unexpected adverse experiences. A copy of any report of unexpected and serious adverse experience associated with use of an IND drug or any finding from tests in laboratory animals that suggests a significant risk for human subjects, which must be reported in writing to FDA as soon as possible but no later than 15 days after the IND sponsor's receipt of the information, must be submitted to the BARDA representative or COR within 24 hours of FDA notification.
  - IDE reports of unanticipated adverse device effect. A copy of any reports of unanticipated adverse device effect submitted to FDA must be submitted to BARDA representative or COR within 24 hours of FDA notification.
  - Expedited safety reports. Sent to BARDA representative or the COR concurrently with the report to FDA.
  - Other adverse events documented during the course of the trial should be included in the annual IND or IDE report and reported to BARDA annually.
- b. Safety reporting for research not performed under an IND or IDE:

Final decisions regarding ongoing safety reporting requirements for research not performed under an IND or IDE must be made jointly by the BARDA PO or the COR and the Contractor.

In case of problems or issues the COR will contact the Contractor within ten (10) working days by email or fax, followed within thirty (30) calendar days by an official letter to the Contractor's Project Manager, with a copy to the institutions' office of sponsored programs, listing issues and appropriate actions to be discussed.

**c. Human Material (Assurance of OHRP Compliance).**

The acquisition and supply of all human specimen material (including fetal material) used under this Contract shall be obtained by Contractor in full compliance with applicable Federal, State and Local laws and the provisions of the Uniform Anatomical Gift Act in the United States, and no undue inducements, monetary or otherwise, will be offered to any person to influence their donation of human material.

The Contractor shall provide written documentation that all human materials obtained as a result of research involving human subjects conducted under this Contract, by collaborating sites, or by subcontractors identified under this Contract, were obtained with prior approval by the Office for Human Research Protections (OHRP) of an Assurance to comply with the requirements of 45 C.F.R. 46 to protect human research subjects. This restriction applies to all collaborating sites without OHRP-approved Assurances, whether domestic or foreign, and compliance must be ensured by Contractor.

Provision by the Contractor to the CO of a properly completed "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310), certifying IRB review and approval of the protocol from which the human materials were obtained constitutes the written documentation required. The human subject certification can be met by submission of a self-designated form provided that it contains the information required by the "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption", Form OMB No. 0990-0263 (formerly Optional Form 310).

## **H.29. FOREIGN TRANSFER OF ASSETS OR TECHNOLOGY**

This clause shall remain in effect during the term of the Contract and for five (5) years thereafter.

**a. Definitions**

**AFFILIATES:** Associated business concerns, non-profit organizations, or individuals if, directly or indirectly, (1) either one controls or can control the other; or (2) a third party controls or can control both.

**ASSET(S):** Tangible or intangible manifestations of technologies having economic value and capable of being conveyed between economic or Governmental entities that is the focus/scope of development by the U.S. Government ("USG") and Contactor in this Contract.

**ASSET(S):** Tangible or intangible manifestations of technologies having economic value and capable of being conveyed between economic or Governmental entities that is the focus/scope of development by the U.S. Government (the "USG") and Contactor in this Contract.

**FOREIGN FIRM OR INSTITUTION:** A firm or institution organized or existing under the laws of a country other than the United States of America (U.S.), its territories, or possessions. The term includes, for purposes of this Contract, any agency or instrumentality of a foreign government; and firms, institutions or business organizations which are owned or substantially controlled by foreign governments, firms, institutions, or individuals.

**TECHNOLOGY:** Technical Data, Computer Software, manufactured materials and Subject Inventions funded by the USG under this Contract. Technology also includes contractor *know how* and personnel expertise, as well as other Assets necessary to assure successful completion of this Contract.

**U.S. FIRM OR INSTITUTION:** A firm or institution organized or existing under the laws of the United States, its territories, or possessions. The term includes, for purposes of this Contract, any agency or instrumentality of the USG; and firms, institutions or business organizations which are owned or substantially controlled by U.S. citizens, firms, institutions, governmental agencies or individuals.

b. General

The parties agree that research findings and technological developments made under this Contract constitute an investment by the USG on behalf of its citizens in the interest of their economic and national health security. These investments are made for the primary benefit of the citizenry of the United States with those same benefits potentially accruing to the people of all nations. Therefore, the USG has a fiduciary responsibility to protect the full invested value of the Assets and Technology developed under this Contract. The USG is also cognizant of the duty the Contractor has to its shareholders and other stakeholders with a vested interest in the economic success of the Contractor. At times both parties are aware their respective interests may diverge. Therefore, in the course of conducting business through the Contract, access to technology developments under this Contract by Foreign Firms or Institutions must be carefully considered.

c. Export Controls

Contractor agrees to comply with all applicable laws regarding export controls and not to export any Asset or Technology to any U.S. embargoed countries.

d. Post-award Transfer of Ownership of Assets or Technology

The Contractor shall provide notice to the CO and COR within three (3) business days of any discussions of a proposed transfer of ownership or establishment of a licensing agreement of any Asset or Technology funded under this Contract from the Contractor to a Foreign Firm or Institution. Notice will also be given within three (3) business days of any discussions of a proposed transfer of operational, corporate, or economic control of Assets and Technology funded under this Contract to Foreign Firms or Institutions. This Article shall not apply to transfers by the Contractor to Affiliated entities of the Contractor, as well as technology transfers for the purposes of manufacturing in accordance with the Statement of Work.

Prior to transferring any Asset funded by the USG under this Contract, the Contractor should carefully review the USG rights under FAR Subpart 42.12 pertaining to Novation, specifically FAR section 42.1204. That provision provides that the USG may recognize a third party assignment only if the transfer of Assets and Technology is determined to be in the USG's interests. The Contractor should be aware that the USG is under **no** obligation to recognize a successor in interest. If the CO determines that a transfer of Assets and Technology may have adverse consequences to the economic well-being or national health security interests of the U.S., the Contractor, and the CO shall jointly endeavor to find alternatives to the proposed transfer which obviate or mitigate potential adverse consequences of the transfer but which may provide substantially equivalent benefits to the Contractor.

In addition to the USG licensing rights to subject inventions and technical data funded under this Contract, see FAR clause 52.227-11 (Patent Rights-Ownership by the Contractor) and FAR Clause 52.227-14 (Rights in Data - General), the USG shall have a first right of refusal for the purchase of the Asset and/or Technology funded under the Contract. The USG may waive this first right of refusal in writing submitted to the Contractor within ninety (90) calendar days of the initial notification to the USG of the Contractor's intent to conduct any form of Asset or corporate transfer.

Except for transfers to affiliates of the Contractor, including those entities necessary to complete the Statement of Work, the Contractor shall provide written notice to the CO and COR of the scheduled transfer to a Foreign Firm or Institution at least ninety (90) calendar days prior to the scheduled date of transfer. Such notice shall cite this Article and shall specifically identify the Asset or Technology proposed for the transfer and the general terms of the transfer. **No transfer shall take place without**

**written concurrence from the CO.**

e. Transfer to a Prohibited Source

In the event of a transfer of an Asset and/or Technology by the Contractor to a Foreign Firm or Institution which is identified as a Prohibited Source pursuant to FAR Subpart 25.7: (a) the USG may terminate this Contract for cause and (b) the license rights to the technical data and subject invention under the relevant FAR IP Clauses (FAR Clause 52.227-11 and FAR Clause 52-227-14) shall survive the termination. Upon request of the USG, the Contractor shall provide written confirmation of such licenses.

a. Lower Tier Agreements

The Contractor shall include this Article, suitably modified, to identify the Parties, in all subcontracts or lower tier agreements, regardless of tier.

### **H.30. PRIORITIES & ALLOCATION SYSTEM**

HHS reserves the right to exercise priorities and allocations authority with respect to this contract, to include rating this order in accordance with 45 CFR Part 101, Subpart A—Health Resources Priorities and Allocations System.

## PART II - CONTRACT CLAUSES

### SECTION I – CONTRACT CLAUSES

#### I.1. FAR 52.252-2, CLAUSES INCORPORATED BY REFERENCE (FEBRUARY 1998)

This contract incorporates the following clauses by reference, with the same force and effect as if they were given in full text. Upon request, the CO will make their full text available. Also, the full text of a clause may be accessed electronically at: <http://www.acquisition.gov/far>. HHSAR clauses at <http://www.hhs.gov/policies/hhsar/subpart352.html>

#### **General Clauses for a Firm Fixed Price Research and Development (R&D) Contract**

a. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES:

Reg	Clause	Date	Clause Title
FAR	52.202-1	Nov 2013	Definitions
FAR	52.203-3	Apr 1984	Gratuities
FAR	52.203-5	May 2014	Covenant Against Contingent Fees
FAR	52.203-6	Sep 2006	Restrictions on Subcontractor Sales to the Government
FAR	52.203-7	May 2014	Anti-Kickback Procedures
FAR	52.203-8	May 2014	Cancellation, Rescission, and Recovery of Funds for Illegal or Improper Activity
FAR	52.203-10	May 2014	Price or Fee Adjustment for Illegal or Improper Activity
FAR	52.203-11	Sept 2007	Certification and Disclosure Regarding Payments to Influence Certain Federal Transactions
FAR	52.203-12	Oct 2010	Limitation on Payments to Influence Certain Federal Transactions
FAR	52.203-13	Oct 2015	Contractor Code of Business Ethics and Conduct
FAR	52.203-14	Oct 2015	Display of Hotline Poster(s)
FAR	52.203-17	Apr 2014	Contractor Employee Whistleblower Rights and Requirement To Inform Employees of Whistleblower Rights
FAR	52.203-19	Jan 2017	Prohibition on Requiring Certain Internal Confidentiality Agreements or Statements
FAR	52.204-4	May 2011	Printed or Copied Double-Sided on Postconsumer Fiber Content Paper
FAR	52.204-7	Jul 2016	System for Award Management
FAR	52.204-8	Oct 2018	Annual Representations and Certifications
FAR	52.204-10	Oct 2016	Reporting Executive Compensation and First-Tier Subcontract Awards
FAR	52.204-13	Oct 2016	System for Award Management Maintenance
FAR	52.204-14	Oct 2016	Service Contract Reporting Requirements
FAR	52.204-16	Jul 2016	Commercial and Government Entity Code Reporting.
FAR	52.204-18	Jul 2016	Commercial and Government Entity Code Maintenance
FAR	52.204-19	Dec 2014	Incorporation by Reference of Representations and Certifications
FAR	52.204-23	Jul 2018	Prohibition on Contracting for Hardware, Software, and Services Developed or Provided by Kaspersky Lab and Other Covered Entities
FAR	52.204-25	Aug 2019	Prohibition on Contracting for Certain Telecommunications and Video Surveillance Services or Equipment

FAR	52.207-1	May 2006	Notice of Standard Competition
FAR	52.209-6	Oct 2015	Protecting the Government's Interests When Subcontracting With Contractors Debarred, Suspended, or Proposed for Debarment
FAR	52.209-9	Jul 2013	Updates of Publicly Available Information Regarding Responsibility Matters
FAR	52.209-10	Nov 2015	Prohibition on Contracting with Inverted Domestic Corporations
FAR	52.210-1	Apr 2011	Market Research
FAR	52.215-2	Oct 2010	Audit and Records – Negotiation
FAR	52.215-8	Oct 1997	Order of Precedence - Uniform Contract Format
FAR	52.215-14	Oct 2010	Integrity of Unit Prices (Over the Simplified Acquisition Threshold
FAR	52.215-22	Oct 2009	Limitations on Pass-Through Charges—Identification of Subcontract Effort
FAR	52.215-23	Oct 2009	Limitations on Pass-Through Charges
FAR	52.219-8	Oct 2014	Utilization of Small Business Concerns
FAR	52.219-28	Jul 2013	Post-Award Small Business Program Representation
FAR	52.222-21	Apr 2015	Prohibition of Segregated Facilities
FAR	52.222-25	Apr 1984	Affirmative Action Compliance
FAR	52.222-35	Oct 2015	Equal Opportunity for Veterans (\$150,000 or more)
FAR	52.222-36	Jul 2014	Equal Opportunity for Workers with Disabilities
FAR	52.222-37	Feb 2016	Employment Reports on Veterans
FAR	52.222-38	Feb 2016	Compliance with Veterans' Employment Reporting Requirements
FAR	52.222-40	Dec 2010	Notification of Employee Rights Under the National Labor Relations Act
FAR	52.222-41	Aug 2018	Service Contract Labor Standards.
FAR	52.222-50	Mar 2015	Combating Trafficking in Persons
FAR	52.222-54	Oct 2015	Employment Eligibility Verification
FAR	52.223-6	May 2001	Drug-Free Workplace
FAR	52.223-18	Aug 2011	Encouraging Contractor Policy to Ban Text Messaging While Driving
FAR	52.225-13	Jun 2008	Restrictions on Certain Foreign Purchases
FAR	52.225-25	Oct 2015	Prohibition on Contracting with Entities Engaging in Certain Activities or Transactions Relating to Iran—Representation and Certifications
FAR	52.226-1	Jun 2000	Utilization of Indian Organizations and Indian-Owned Economic Enterprises.
FAR	52.227-1	Dec 2007	Authorization and Consent, Alternate 1 (APR 1984)
FAR	52.227-2	Dec 2007	Notice and Assistance Regarding Patent and Copyright Infringement
FAR	52.227-3	Apr 1984	Patent Indemnity ALT 1
FAR	52.227-11	May 2014	Patent Rights – Ownership by the Contractor
FAR	52.227-14	May 2014	Rights in Data – General
FAR	52.227-15	Dec 2007	Representation of Limited Rights Data and Restricted Computer Software
FAR	52.227-16	June 1987	Additional Data Requirements

FAR	52.228-7	Mar 1996	Insurance – Liability to Third Persons
FAR	52.229-3	Feb 2013	Federal, State, and Local Taxes.
FAR	52.232-2	Apr 1984	Payments Under Fixed-Price Research and Development Contracts
FAR	52.232-20	Apr 1984	Limitation of Cost
FAR	52.232-23	May 2014	Assignment of Claims
FAR	52.232-25	Jan 2017	Prompt Payment
FAR	52.232-33	Jul 2013	Payment by Electronic Funds Transfer–System for Award Management
FAR	52.232.39	Jun 2013	Unenforceability of Unauthorized Obligations
FAR	52.232-40	Dec 2013	Providing Accelerated Payments to Small Business Subcontractors
FAR	52.233-1	May 2014	Disputes
FAR	52.233-2	Sep 2006	Service of Protest
FAR	52.233-3	Aug 1996	Protest After Award
FAR	52.233-4	Oct 2004	Applicable Law for Breach of Contract Claim
FAR	52.242-1	Apr 1984	Notice of Intent to Disallow Costs
FAR	52.242-3	May 2014	Penalties for Unallowable Costs
FAR	52.242-4	Jan 1997	Certification of Final Indirect Costs
FAR	52.242-13	Jul 1995	Bankruptcy
FAR	52.242-15	Aug 1989	Stop Work Order
FAR	52.243-1	Aug 1984	Changes – Fixed Price Alternate V
FAR	52.244-2	Oct 2010	Subcontracts, Alternate 1 (Jun 2007)
FAR	52.244-5	Dec 1996	Competition in Subcontracting
FAR	52.244-6	Jan 2019	Subcontracts for Commercial Items
FAR	52.245-1	Apr 2012	Government Property
FAR	52.245-9	Apr 2012	Use and Charges
FAR	52.246-4	Aug 1996	Inspection of Services -- Fixed-Price
FAR	52.246-7	Aug 1996	Inspection of Research and Development -- Fixed-Price
FAR	52.246-9	Aug 1989	Inspection of Research and Development (Short Form)
FAR	52.246-16	Aug 1984	Responsibility for Supplies
FAR	52.246-23	Feb 1997	Limitation of Liability
FAR	52.249-2	Apr 2012	Termination for Convenience of the Government (Fixed-Price)
FAR	52.249-9	Apr 1984	Default (Fixed-Price Research and Development)
FAR	52.253-1	Jan 1991	Computer Generated Forms

b. DEPARTMENT OF HEALTH AND HUMAN SERVICES ACQUISITION REGULATION (HHSAR) (48 CFR CHAPTER 3) CLAUSES:

Reg	Clause	Date	Clause Title
HHSAR	352.203-70	Dec 2015	Anti-Lobbying
HHSAR	352.208-70	Dec 2015	Printing and Duplication
HHSAR	352.211-3	Dec 2015	Paperwork Reduction Act
HHSAR	352.222-70	Dec 2015	Contractor Cooperation in Equal Employment Opportunity Investigations
HHSAR	352.223-70	Dec 2015	Safety and Health
HHSAR	352.224-70	Dec 2015	Privacy Act
HHSAR	352.224-71	Dec 2016	Confidential Information

HHSAR	352.227-70	Dec 2015	Publications and Publicity
HHSAR	352.233-70	Dec 2015	Choice of Law (Overseas)
HHSAR	352.237-75	Dec 2015	Key Personnel
HHSAR	352.231-70	Dec 2015	Salary Rate Limitation
HHSAR	352.239-74	Dec 2015	Electronic and Information Technology Accessibility
HHSAR	352.270-5b	Dec 2015	Care of Live Vertebrate Animals.
HHSAR	352.270-6	Dec 2015	Restriction on Use of Human Subjects.
HHSAR	352.270-9	Dec 2015	Non-discrimination for Conscience
HHSAR	352.270-13	Dec 2015	Continued Ban on Funding Abortion and Continued Ban on Funding of Human Embryo Research.

## I.2. ADDITIONAL FAR CONTRACT CLAUSES INCLUDED IN FULL TEXT

This contract incorporates the following clauses in full text. FEDERAL ACQUISITION REGULATION (FAR) (48 CFR CHAPTER 1) CLAUSES:

### FAR Clause 52.219-28, Post-Award Small Business Program Representation (July 2013)

a. *Definitions* . As used in this clause--

*Long-term contract* means a contract of more than five years in duration, including options. However, the term does not include contracts that exceed five years in duration because the period of performance has been extended for a cumulative period not to exceed six months under the clause at 52.217-8, Option to Extend services, or other appropriate authority.

*Small business concern* means a concern, including its affiliates that is independently owned and operated, not dominant in the field of operation in which it is bidding on Government contracts, and qualified as a small business under the criteria in 13 CFR part 121 and the size standard in paragraph (c) of this clause. Such a concern is "not dominant in its field of operation" when it does not exercise a controlling or major influence on a national basis in a kind of business activity in which a number of business concerns are primarily engaged. In determining whether dominance exists, consideration shall be given to all appropriate factors, including volume of business, number of employees, financial resources, competitive status or position, ownership or control of materials, processes, patents, license agreements, facilities, sales territory, and nature of business activity.

b. If the Contractor represented that it was a small business concern prior to award of this contract, the Contractor shall re-represent its size status according to paragraph (e) of this clause or, if applicable, paragraph (g) of this clause, upon the occurrence of any of the following:

(1) Within 30 days after execution of a novation agreement or within 30 days after modification of the contract to include this clause, if the novation agreement was executed prior to inclusion of this clause in the contract.

(2) Within 30 days after a merger or acquisition that does not require a novation or within 30 days after modification of the contract to include this clause, if the merger or acquisition occurred prior to inclusion of this clause in the contract.

(3) For long-term contracts--

- (i) Within 60 to 120 days prior to the end of the fifth year of the contract; and
- (ii) Within 60 to 120 days prior to the date specified in the contract for exercising any option thereafter.



- c. The Contractor shall represent its size status in accordance with the size standard in effect at the time of this re-representation that corresponds to the North American Industry Classification System (NAICS) code assigned to this contract. The small business size standard corresponding to this NAICS code can be found at <http://www.sba.gov/content/table-small-business-size-standards>
- d. The small business size standard for a Contractor providing a product which it does not manufacture itself, for a contract other than a construction or service contract, is 500 employees.
- e. Except as provided in paragraph (g) of this clause, the Contractor shall make the representation required by paragraph (b) of this clause by validating or updating all its representations in the Representations and Certifications Section of the System for Award Management (SAM) and its other data in SAM, as necessary, to ensure that they reflect the Contractor's current status. The Contractor shall notify the contracting office in writing within the timeframes specified in paragraph (b) of this clause that the data have been validated or updated, and provide the date of the validation or update.
- f. If the Contractor represented that it was other than a small business concern prior to award of this contract, the Contractor may, but is not required to, take the actions required by paragraphs (e) or (g) of this clause.
- g. If the Contractor does not have representations and certifications in SAM, or does not have a representation in SAM for the NAICS code applicable to this contract, the Contractor is required to complete the following representation and submit it to the contracting office, along with the contract number and the date on which the representation was completed:

The Contractor represents that it ☒ is, ☐ is **not** a small business concern under NAICS Code 541715 assigned to this contract.

(End of clause)

#### **FAR 52.204-21 Basic Safeguarding of Covered Contractor Information Systems (Jun 2016)**

(a) *Definitions.* As used in this clause--

“Covered contractor information system” means an information system that is owned or operated by a contractor that processes, stores, or transmits Federal contract information.

“Federal contract information” means information, not intended for public release, that is provided by or generated for the Government under a contract to develop or deliver a product or service to the Government, but not including information provided by the Government to the public (such as on public Web sites) or simple transactional information, such as necessary to process payments.

“Information” means any communication or representation of knowledge such as facts, data, or opinions, in any medium or form, including textual, numerical, graphic, cartographic, narrative, or audiovisual (Committee on National Security Systems Instruction (CNSSI) 4009).

“Information system” means a discrete set of information resources organized for the collection, processing, maintenance, use, sharing, dissemination, or disposition of information (44 U.S.C. 3502).

“Safeguarding” means measures or controls that are prescribed to protect information systems.

(b) Safeguarding requirements and procedures.

(1) The Contractor shall apply the following basic safeguarding requirements and procedures to protect covered contractor information systems. Requirements and procedures for basic safeguarding of covered contractor information systems shall include, at a minimum, the following security controls:

- (i) Limit information system access to authorized users, processes acting on behalf of authorized users, or devices (including other information systems).
- (ii) Limit information system access to the types of transactions and functions that authorized users are permitted to execute.
- (iii) Verify and control/limit connections to and use of external information systems.
- (iv) Control information posted or processed on publicly accessible information systems.
- (v) Identify information system users, processes acting on behalf of users, or devices.
- (vi) Authenticate (or verify) the identities of those users, processes, or devices, as a prerequisite to allowing access to organizational information systems.
- (vii) Sanitize or destroy information system media containing Federal Contract Information before disposal or release for reuse.
- (viii) Limit physical access to organizational information systems, equipment, and the respective operating environments to authorized individuals.
- (ix) Escort visitors and monitor visitor activity; maintain audit logs of physical access; and control and manage physical access devices.
- (x) Monitor, control, and protect organizational communications (i.e., information transmitted or received by organizational information systems) at the external boundaries and key internal boundaries of the information systems.
- (xi) Implement subnetworks for publicly accessible system components that are physically or logically separated from internal networks.
- (xii) Identify, report, and correct information and information system flaws in a timely manner.
- (xiii) Provide protection from malicious code at appropriate locations within organizational information systems.
- (xiv) Update malicious code protection mechanisms when new releases are available.
- (xv) Perform periodic scans of the information system and real-time scans of files from external sources as files are downloaded, opened, or executed.

- a. *Other requirements.* This clause does not relieve the Contractor of any other specific safeguarding requirements specified by Federal agencies and departments relating to covered contractor information systems generally or other Federal safeguarding requirements for controlled unclassified information (CUI) as established by Executive Order 13556.

(c) *Subcontracts.* The Contractor shall include the substance of this clause, including this paragraph (c), in subcontracts under this contract (including subcontracts for the acquisition of commercial items, other than commercially available off-the-shelf items), in which the subcontractor may have Federal contract information residing in or transiting through its information system.

(End of clause)

#### **FAR 52.227-7 Patents – Notice of Government License (APR 1984)**

The Government is obligated to pay a royalty applicable to the proposed acquisition because of a license agreement between the Government and the patent owner. The patent number is \_\_\_\_ [Contracting Officer fill in], and the royalty rate is \_\_\_\_ [Contracting Officer fill in]. If the offeror is the owner of, or a licensee under, the patent, indicate below:

- ☐ **Owner**
- ☐ **Licensee**

If an offeror does not indicate that it is the owner or a licensee of the patent, its offer will be evaluated by adding thereto an amount equal to the royalty

(End of clause)

## **I.2. ADDITIONAL HHSAR CONTRACT CLAUSES INCLUDED IN FULL TEXT**

### **HHSAR 352.231-70 – Salary Rate Limitation (December 18, 2015)**

- i. Pursuant to the current and applicable prior HHS appropriations acts, payment of the direct salary of an individual at a rate in excess of the Federal Executive Schedule Level II in effect on the date Government funding was obligated.
- ii. For purposes of the salary rate limitation, the terms “direct salary,” “salary”, and “institutional base salary”, have the same meaning and are collectively referred to as “direct salary”, in this clause. An individual’s direct salary is the annual compensation that the Recipient pays for an individual’s direct effort (costs) under the contract. Direct salary excludes any income that an individual may be permitted to earn outside of duties to the Recipient. Direct salary also excludes fringe benefits, overhead, and general and administrative expenses (also referred to as indirect costs or facilities and administrative [F&A] costs).

Note: The salary rate limitation does not restrict the salary that an organization may pay an individual working under a Government contract, order, or OTAR; it merely limits the portion of that salary that may be paid with Federal funds.

- iii. The salary rate limitation also applies to individuals under Sub-Recipient Agreements except to the extent that that a Sub-Recipient Agreement is awarded on a fixed-price basis without analysis of labor costs. If this is a multiple-year contract, it may be subject to unilateral modification by the CO to ensure that an individual is not paid at a rate that exceeds the salary rate limitation provision established in the HHS appropriations act in effect when the expense is incurred regardless of the rate initially used to establish Agreement funding.
- iv. See the salaries and wages pay tables on the U.S. Office of Personnel Management Web site for Federal Executive Schedule salary levels that apply to the current and prior periods

(End of clause)

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### **PART III - LIST OF DOCUMENTS, EXHIBITS AND OTHER ATTACHMENTS**

#### **SECTION J - LIST OF ATTACHMENTS**

The following documents are attached and incorporated in this contract:

1. Statement of Work, dated 27-July-2020
2. Sample Invoice/Financial Request Instructions
3. Schedule of Payments
4. Reporting Deliverable Table - Contractor Locations and Product Development Source Material

### **PART IV - REPRESENTATIONS AND INSTRUCTIONS**

#### **SECTION K - REPRESENTATIONS, CERTIFICATIONS AND OTHER STATEMENTS OF OFFERORS**

The following documents are incorporated by reference in this contract:

- a. Animal Research Assurance Identification Numbers: To be provided prior to study execution.
- b. Human Subjects Assurance Identification Numbers: To be provided prior to study execution.

Pursuant to 45 CFR part 46, Protection of Human Research Subjects, the Contractor shall not expend funds under this award for research involving human subjects or engage in any human subject research activity prior to the Contracting Officer's receipt of a certification that the research has been reviewed and approved by the Institutional Review Board (IRB) registered with OHRP. This restriction applies to all collaborating sites, whether domestic or foreign, and subcontractors. The Contractor must ensure compliance by collaborators and subcontractors.

## **Attachment 1**

### **Biomedical Advanced Research and Development Authority (BARDA) Broad Agency Announcement BAA-20-100-SOL-0002**

EgressRD - mRNA oral cellular vaccine  
delivery technology

#### **Area of Interest #4.3 (COVID-19)**

#### **Statement of Work (SOW)**

**July 27, 2020**

#### **PREAMBLE**

Independently, and not as an agent of the government, the contractor shall furnish all necessary services; qualified professional, technical, and administrative personnel; and material, equipment, and facilities not otherwise provided by the government under the terms of this contract, as needed to perform the tasks set forth below.

The government reserves the right to modify the budget, progress, schedule, or milestones to add or delete processes, schedules, or deliverables if the need arises. Because of the nature of this research and development (R&D) contract and the complexities inherent in this and prior programs, at designated milestones the government will evaluate whether work should be redirected or removed, or whether schedule or budget adjustments should be made. The government reserves the right to change the product, process, schedule, or events to add or delete part or all of these elements as the need arises.

#### **Overall Objectives and Scope**

The overall objective of this contract is to demonstrate proof-of-concept for our mRNA oral cellular vaccine delivery technology - Egress<sup>RD</sup> - for a specific viral disease: COVID-19. Our genetically modified strain of yeast, *Saccharomyces cerevisiae*, produces enveloped virus-like particles (VLPs) and delivers the genetic instructions for the expression of target SARS-CoV-2 viral antigens to the patients' gut cells, where immunity may commence and become manifest.

The scope of work for this contract includes constructing yeast strains to find the most compatible antigen mRNA VLP producers, followed by immunogenicity studies in mice in vivo efficacy testing in hamsters to establish the successful candidates' ability to elicit a detectable immune response and provide protection against disease and potentially transmission.

The R&D effort for Oral mRNA Cellular Vaccine for COVID-19 will progress in work segments with key Deliverables being due during the Base Period of performance of the contract (the Base Period will be labeled Contract Line Item Number (CLIN) 0001). Each Deliverable includes concrete work segments with well-defined objectives, scopes of work, and success metrics for accomplishing the Deliverable.

The Deliverables for this project are described below:

1. **Deliverable 1** – Construction of yeast strains to find the most compatible antigen mRNA VLP producers.
2. **Deliverable 2** – Completion of immunogenicity studies in mice and in vivo efficacy testing in hamsters (and final report)

## 1. Deliverable 1: Construction of yeast strains to find the most compatible antigen mRNA VLP producers

### Objective:

The main objective is to construct yeast strains to find the most compatible antigen mRNA-VLP(RVLP) producers

### Scope of Work:

Most of the candidate vaccines against COVID-19 aim to induce neutralizing antibodies against the SARS-CoV-2 viral spike (S) protein, blocking the pathogen's entrance through the ACE2 portal. However, recent experience with SARS-CoV-1 vaccine development indicated anti-spike IgG can enhance the inflammatory response through antibody dependent enhancement (ADE); for this purpose, we are including all three structural proteins of SARS-CoV-2 (S, E and M protein) into our vaccine development, with S protein receiving priority. HexaPro (see reference), an engineered spike protein variant with 6 proline substitutions that increase expression and stability, will be used to construct the S protein- expressing yeast construct.

- 1.1 *Synthesis and design of RVLP construct:* Delivering SARS-CoV-2-RVLPs using Egress<sup>RD</sup> platform will require stable expression or plasmid-based expression of (i) Esperovax proprietary egress1 protein (ii) GAGMS2, GAG capsid protein from human immunodeficiency virus is fused to MS2, bacteriophage capsid protein (Carrier), (iii) each of the candidate antigens SARS-CoV-2 protein which will be fused to 12 or 24 MS2 binding sites in the 3' end (referred as Cargo). RVLP plasmid will be constructed by cloning three different expression cassettes in proprietary 2-micron yeast expression vector: 1) Galp -Egress1-Cyct 2) Adh2p-GAGMS2-Adht and 3) ADH2p-eGFP12X or 24XM2 -ADHt (GFP-RVLPs). The first two cassettes will be common for each construct, and the third cassette will carry the mRNA sequence of the GFP reporter gene. The GFP strain will be used to determine the efficiency of mRNA encapsulation into VLPs, (12x or 24x) This third cargo cassette will then be replaced with mRNA sequences for S, E and M antigens of SARS-CoV-2 with 12 or 24 MS2 binding sites to generate (COVS\_RVLPs), (COVE\_RVLPs) and (COVM\_RVLPs) respectively. Total we will generate 5 constructs with cargos containing 12 or 24 MS2 binding sites. *S. cerevisiae*, BY4742 strain will be transformed with RVLP vectors carrying 5 constructs. using standard electroporation protocol or quick transformation kit (Cat #631851, Takara). Transformants colonies will be selected on uracil drop out YNB medium.

As an alternate strategy to obtain a more stable cell line, we will integrate these three genes into the yeast genome. We will employ clustered regularly interspaced short palindromic repeats and CRISPR-associated protein- 9 nuclease (CRISPR-cas9) genome editing tool. CRISPR-Cas9 mediated DSBs at specific repetitive regions (delta sites; a long terminal repeat associated with Ty elements of yeast) will be created by transforming yeast with pDi-CRISPR plasmid comprised of a specific delta-targeting guide RNA and a Cas9 nuclease. These breaks will be repaired by non-homologous end joining (NHEJ) or homology directed repair (HDR) pathways. Donor DNA template that matches the DNA sequence on either side of the DSB is widely employed to insert DNA sequence of interest into genome at DSBs generated by CRISPR-Cas9. The pDi-CRISPR plasmid will be constructed using pCRCT plasmid (obtained from Dr. Humin Zhao under MTA) by introducing a specific guide RNA sequence. Donor DNA with different expression cassettes and DNA sequences that matches the 2- halves of the DSB site of delta sequences at each end (Figure1) will be synthesized by Vector Builder (Table1). Egress1 and GAG/MS2 genes will be codon optimized for yeast however codon optimization of SARS-CoV-2 genes encoding for yeast is not necessary as they are targeted to be translated inside human enterocytes. The pDi-CRISPR plasmid and linearized donor DNA plasmid carrying expression cassettes with DNA sequences that matches the 2- halves of the DSB site of delta sequences at each end will be linearized and co-transformed into BY4742 *S. cerevisiae* yeast strain (MATa; his3D1; leu2D0; lys2D0; ura3D0) using the LiAc/SS carrier DNA/PEG method. This

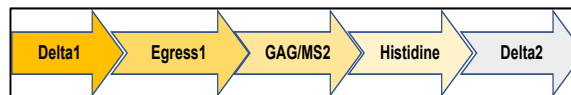


Figure 1. Design scheme of a donor DNA sequence<sup>13</sup>.

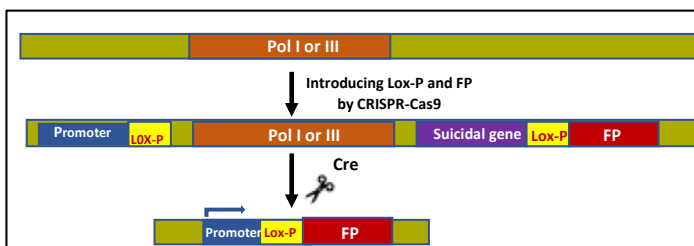
Table 1. List of donor DNA constructs for integration	
RVLPs	Donor DNA sequences for integration in yeast genome
1	Delta 1-E1+GAGMS2+eGFP cargo 12 XM2 +His-Delta2 2
2	Delta 1-E1+GAGMS2+eGFP cargo 24 XM2 +His-Delta2 2
3	Delta1-E1 +GAGMS2+ COV_S 12X M2 +His-Delta2
4	Delta1-E1 +GAGMS2+ COV_M 12 X M2 +His-Delta2
5	Delta1-E1 +GAGMS2+ COV_E 12X M2 +His-Delta2
6	Delta1-E1 +GAGMS2+ COV_S 24X M2 +His-Delta2
7	Delta1-E1 +GAGMS2+ COV_M 24X M2 +His-Delta2
8	Delta1-E1 +GAGMS2+ COV_E 24X M2 +His-Delta2

will allow integration of multiple copies of donor DNA into yeast genome via homologous recombination at the DSBs of delta sites. YNB with Ura and His dropout media will be used to select integrants yeast with RVLP constructs as the BY4742 yeast strain is auxotrophic to uracil and histidine.

- 1.2 *Production of RVLPs in yeast:* Plasmid transformants (Ura dropout YNB media) or genome integrant, (Ura and His drop out YNB media) yeast clones will be selected on respective selection media for screening the secretion of RVLPs. Overnight grown yeast clones (day1) in selection media (preculture) will be sub cultured in 3 ml cultures to OD<sub>600</sub>=0.5-1.0, in uracil and leucine deficient (-Ura, -Leu) YNB 2% glucose media (amplification culture) to allow selection of cells harboring high plasmid copy (day 2). The amplification culture will be diluted to 2XYNB (-Ura, -Leu) +2% glucose media containing 1.0M sorbitol (induction media) with initial OD<sub>600</sub>=2 (day3). The carrier protein (GAG/MS2) and SARS- CoV-2 antigen RNA genes will be expressed under ADH2 promoter, (which is tightly repressed by glucose in the growth medium and induction of gene occurs when glucose is exhausted ref). The Egress1 protein is expressed under Gal1 promoter, therefore the addition of galactose will induce Egress1 protein when glucose is exhausted from the culture media. RVLP expression will be monitored after glucose is exhausted and galactose is added by time course analysis of samples taken at every 8 h interval for up to 72 h (post induction time). Supernatant from yeast culture / yeast transformant (8 clones) clones from each construct will be clarified to remove cells and processed to extract RNA from VLPs. The yeast clones expressing RVLPs with packaged mRNA will be screened by RT-PCR using gene specific primers for respective antigen genes.
- 1.3 *Purification of RVLPs:* Positive yeast clones carrying COVID-19 RVLPs (confirmed by RT-PCR) will be grown to 100 ml volume of induction media after preculture and amplification growth. The secreted RVLPs into the fermented yeast media will be clarified by centrifugation. Clarified culture media will be centrifuged through 30% wt/vol sucrose at 4°C at 26,000 rpm for 1.5 hours. The pellet containing RVLPs will be resuspended in PBS and subjected to 20-70% sucrose gradient at 35,000 rpm for 16 hours. The fractions containing purified RVLPs will be pooled and used for characterization studies.
- 1.4 *Transmission electron microscopic studies of RVLP formation:* TEM analysis will be performed to study the formation of RVLPs carrying mRNA of SARS-CoV-2 for their integrity and morphology. TEM studies will be performed with yeast for budding RVLPs at different phases of expression as well as for purified secreted RVLPs from the fermentation media. After induction, the samples will be removed at different time points during the fermentation process for quantitative analysis of the yeast expressing RVLPs. Yeast cells will be fixed in 100 mM cacodylate buffer, pH 7.2, containing 2% glutaraldehyde and followed with 1% osmium tetroxide for TEM studies. From purified RVLPs, 10 µL samples will be adsorbed onto a formvar coated 150 mesh copper grids from Veco (Science Services, Germany) for 2 minutes. Then the grid will be washed five times with sterile filtered dH<sub>2</sub>O, soaked in 2% uranyl acetate solution for 2 min and dried in air at room temperature to follow TEM studies. The clones showing VLP formation confirmed by TEM studies will be used for in Vitro transduction studies.
- 1.5 *Analysis of RVLPs in vitro:* Purified SARS-CoV-2-RVLPs will be tested for their ability to deliver translatable specific SARS-CoV-2 antigen in mouse dendritic cell line (DC2.4; Sigma, St. Louis, MO). DC2.4 cells will be cultured in Eagle's Minimum Essential Medium supplemented with 10% fetal bovine serum (FBS) and supplemented with penicillin/ streptomycin solution and grown at 37°C in a CO<sub>2</sub> chamber. To optimize transduction efficiency of RVLPs, DC2.4 will be seeded onto 6-well plates at a density of 1x10<sup>6</sup> cells/well in above medium and incubated at 37°C overnight. Before transduction, the medium will be removed, and the cells will be washed twice with sterile PBS. Then the cells will be transduced with SARS-CoV-2-RVLPs carrying mRNA encoding for SARS-CoV-2 antigen or GFP-RVLPs (as an internal control) at different dilutions (1:10; 1: 20; 1:40; 1:80 and 1:100) in 2 ml culture medium and incubated as above for 24 h. To test the transduction efficiency of RVLPs, DC2.4 cells will be analyzed for the expression of SARS-CoV-2 antigen(s) by Western blot analysis using anti-SARS-CoV-2 specific antibodies. Further, immunolocalization of SARS-CoV-2 proteins in DC2.4 cells will be also performed using anti-SARS-CoV-2 specific antibodies followed by anti-IgG-Alexa flour conjugated secondary antibodies under Fluorescent phase contrast microscope.
- 1.6 *Seed stock production:* Merck USA has agreed to produce and characterize the seed stocks of positive strains, as well as prepare sufficient quantities in their GLP manufacturing facility in Scotland for pre-clinical and early clinical development. Pending results of the animal immunogenicity and challenge studies with SARS-CoV-2 virus, stable master and working cell banks will be established and toxicology studies will ensue in parallel to

support an Investigational New Drug (IND) application to the FDA to permit Phase 1 safety and dose-ranging clinical studies in humans. Upon IND acceptance by the FDA, additional funding will be requested to support human clinical trials and related work.

- 1.7 Viability Switch (VS<sup>TM</sup>): Use of genetically modified (GM) yeast for oral delivery could be a limitation for FDA approval. To mitigate this risk, we designed a VS<sup>TM</sup> in recombinant yeast. The VS<sup>TM</sup> will be genetically introduced in GM yeast expressing RVLPs, designed to turn off the cell division by knocking out DNA polymerase I and III (Pol I and III). This will be achieved by using Cre-lox P system, introducing lox-P sites (-1 and -2) on either side of one of Pol I or III using CRISPR-Cas9 genome editing tool. Figure 2 describes strategy for designing a viability switch. Expression of Cre-recombinase lead to expression of fluorescent protein (FP) only in the DNA polymerase knock-out cells and these cells can be isolated by a simple technique like Fluorescent Activated Cell Sorting (FACS) or a similar approach and will be ready to use for oral delivery. Suicidal gene will be induced for negative selection against cell lines with negative knockouts.



**Figure 2.** Schematic representation of yeast viability switch. (A) Yeast DNA polymerase I or III gene locus, (B) Lox-P sites-1 and native yeast promoter into upstream and, suicidal gene, Lox-P site-2 and RFP by CRISPR-Cas 9 into downstream of Pol I or III, (C) Knocked out DNA Pol I/III and suicidal gene.

#### Success Metric for Completion of Deliverable 1:

Simultaneous expression of three genes: Egress1, Carrier protein (GAGMS2) and cargo containing SARS-CoV-2 antigen mRNA by using 2u plasmid will provide yeast clone secreting SARS-CoV-2-RVLPs S, E and M antigens.

The validation of size and sequence of RT PCR products from RVLPs will confirm the accuracy of packaging mRNA in to RVLPs as GFP mRNA was packaged in prototype RVLPs in yeast without degradation.

In general, use of 2μ plasmid yields 50-200 copies of gene /cell which obtains 200 mgs-1 g of protein expression in yeast cells. Therefore, we expect to have at-least 50-100 mg /L of RVLPs produced in yeast which will enable the characterization and in vitro studies.

The formation and morphology of *RVLP*: TEM studies will confirm assembly of RVLPs which should be similar to MS2 VLP expressed in *S cerevisiae* (ref).

We expect to reproduce *in vitro* data on RVLP prototype (eGFP mRNA) and demonstrate RVLPs of SARS-CoV-2 antigens will be taken up, unpackaged, and translated into respective protein inside DC2.4 cell. The SARS-CoV-2 S, E and M antigens expressed in DC2.4 cells from processing of RVPs will be confirmed by western blot analysis.

We anticipate that dendritic cells transduced with RVLPs will express SARS-CoV-2 antigen(s) in sufficient quantities required for efficacy studies in animals by oral route.

#### Risk mitigation:

In case if the RVLPs fails to produce sufficient quantity of SARS-CoV-2 antigens, we propose to use Self-amplifiable mRNAs (SAM)-based RVLPs (AVLPs) approach to increase the magnitude of antigen expression *in vivo*. SAMs have been widely used for mRNA-based vaccine development and proven to have higher levels of antigen expression and high degrees of efficacy. AVLPs based vaccine provide protection with much lower doses and is very safe to deliver as the VLPs lack endogenous viral structural genes.

Designing non-dividing a yeast cell line to ensure safe use of Egress<sup>RD</sup> platform. This will ensure the safe use of the vaccine and eliminate the risk of release of GM yeast into the environment.



## **Deliverable 2: Completion of immunogenicity in mice and in vivo efficacy testing in hamsters**

### **Objective: Immunogenicity and Efficacy testing of SARS-CoV-2-RVLPs producing yeast in mice and hamsters**

#### **Scope of Work:**

Several recent studies signify that mRNA-based vaccines can provide protection against influenza virus infection, and mRNA-based influenza virus vaccines elicited broadly reactive antibodies capable of neutralizing viruses (Pardi, N. et al. 2018). An encapsulated mRNA-based vaccine protected mice and non-human primates against Zika virus infection after a single low dose immunization (Pardi, N. et al. 2017). RNA-based prophylactic drugs /vaccines have demonstrated therapeutic efficacy in preclinical animal models and in clinical trials (Lundstrom, 2018). In this study, we propose to orally administer mice and hamsters with SARS-CoV-2-RVLPs secreting yeast to elicit a detectable immune response (mice) and protection from viral challenge (hamsters). Hamsters have been successfully used as a preclinical animal model to study SARS-CoV-2 virus infection and pathogenicity (*Juergen Richt, 2020*). Anti-sera from the animal models will be screened for antigen-specific antibodies by ELISA, and for neutralizing antibodies SARS-CoV-2 virus in micro-neutralization tests.

*Oral Immunization of mice with yeast secreting SARS-CoV-2-RVLPs using a monovalent S-Protein, and a multivalent with the s-Protein and either the E protein or M protein (choosing only one based on the immunogenicity studies):* Six-week-old female BALB/c mice (Jackson Laboratory, Bar Harbor, ME) will be used in this study. Prior to immunization, baseline body weights will be measured. Ten mice per group will be anesthetized with isoflurane, and administered low, medium, and high doses ( $10^4$ ,  $10^5$ ,  $10^6$  cells) of a yeast strain secreting SARS-CoV-2-RVLPs by oral intragastric gavage in 0.2 to 0.3 ml sterile saline solution on day 0 and day 21. On days 28 and 42 post-immunization, 5 mice each will be euthanized by isoflurane overdose and blood will be harvested for antibody titer. On day 21, 12-24 hrs post-boost (2<sup>nd</sup> dose), TH1 (e.g., IFN- $\gamma$ ) and TH2 (IL-4) cytokine analysis will be done by harvesting splenocytes and re-stimulating them in vitro with the respective antigen. Production of IFN- $\gamma$  (TH1) and IL-4 (TH2) by the spleen cells will be either measured by ELISPOT (IFN- $\gamma$  and IL-4 antibodies) or by measuring the cytokine production with ELISA kits for IFN- $\gamma$  and IL-4. Another group of mice (n=10) will be given only saline solution or “empty yeast” similar as above and will serve as the negative controls.

*Oral Immunization of hamsters with yeast cells secreting SARS-CoV-2-RVLPs and SARS-CoV-2 challenge:* 6-10-week-old male hamsters (Jackson Laboratories; Charles River) which are serologically negative for SARS-CoV-2 will be enrolled in the study. Baseline body weights will be established by multiple measurements prior to immunization. Three groups of 6-8 hamsters per group will be anesthetized with isoflurane, and administered previously determined antibody inducing doses of yeast cells secreting SARS-CoV-2 RVLPs (containing SARS-CoV-2 antigen mRNA) or saline solution/“empty” yeast by oral intragastric gavage in 0.5 to 1 ml sterile saline solution on day 0 and day 21. Body weight and survival will be monitored daily. Vaccinated hamsters and the control mock-vaccinated group will be challenged 2 weeks after the booster inoculation (i.e. day 35) with  $10^5$  TCID<sub>50</sub> SARS-CoV-2 (USA-MA1/2020) by intranasal application. On day two or three post infection, three hamsters from each group will be euthanized by isoflurane overdose and blood and tissues samples will be harvested for pathologic examination and for determination of the presence of viral RNA/virus. Body weight, clinical signs and survival will be monitored daily. Animals losing >20% body weight have to be humanely euthanized. All surviving hamsters will be euthanized by isoflurane overdose on day 14 post infection, and blood and tissues samples will be harvested for virologic and pathologic examinations, and for antibody titer analysis.

*Enzyme-linked immunosorbent assay:* Specific anti-SARS-CoV-2 IgG antibodies will be detected through in-house prepared or a commercial (Sino Biological Inc) ELISA kits based on the SARS-CoV-2 S1 protein or the RBD of the spike protein. ELISA plates pre-coated with recombinant S1, RBD, M, or E proteins of SARS-CoV-2 will be utilized in this study as determined through in-house validations or per vendor instructions. The assays will provide semi-quantitative results by calculating the ratio of the OD of the serum sample over the OD of the calibrator. The cut-off for a sample being called positive is determined as follows: Average OD of negative serum + 3X STDEV. Everything above this cut-off is considered as positive.

**SARS-CoV-2 neutralization CPE assay:** A neutralization assay with authentic SARS-CoV-2 virus (USA-WA1/2020 strain) will be performed with cytopathic effect (CPE) as a read-out. Briefly, various dilutions of heat-inactivated (56°C for 30 minutes) sera (1:2 dilutions in DMEM) will be mixed with the same volume of 100 PFU/TCID<sub>50</sub> of SARS-CoV-2 and incubated at 37°C for 1 h. The mixture will then be added to a monolayer of Vero-E6 cells (5x10<sup>3</sup> cell per well) in a 96-well plate and incubated for 1 h at 37°C. The supernatant will be removed, and 200 µL of DMEM supplemented with 2% (v/v) FBS will be added onto the infected cells. After incubation at 37°C supplied with 5% CO<sub>2</sub> for 3-5 days, all wells will be examined for CPE. All experiments will be performed in a Biosafety Level 3+ facility @ KSU (Juergen Richt). The average of duplicate results will be used to determine the final NT<sub>50</sub> titer. The neutralizing antibody titer NT<sub>50</sub> is shown as the reciprocal of the average serum dilution at which no CPE breakthrough in any of the testing wells is observed.

#### **Success Metric for Completion of Deliverable 2:**

We expect to demonstrate that yeast cells secreting SARS-CoV-2-RVLPs elicit a strong immune response with high titers of neutralizing antiserum for protection against anti-SARS-CoV-2 in both mice and hamsters. Further, we anticipate that immunization of hamsters with yeast cells secreting SARS-CoV-2-RVLPs will provide protection against lethal SARS-CoV-2 challenge; and we predict that the protective efficacy of the yeast vaccine is dose-dependent (low versus high dose). We will examine the vaccinated and control hamsters challenged with SARS-CoV-2 (USA-WA1/2020 isolate) daily for clinical signs, such as weight loss, ruffled fur, huddling and inactivity; and will analyze their lung tissues for the presence of viral antigen/RNA or excessive IgGs and infiltrating immune cells (B/T lymphocytes, macrophages, neutrophils) by IHC/RNA Scope and H&E, respectively. Animals that show no signs of disease for 14 days post challenge will be considered protected. These experiments will result in a pre-clinical test of one or more RVLPs-based vaccine candidate against SARS-CoV2 *in vivo*.

No potential problems are anticipated in eliciting immune response against RVLPs-based SARS-CoV-2 antigen(s) *in vivo* models since we have successfully demonstrated anti-eGFP antibody titer in mice immunized with RVLPs of eGFPs. However, if the BALB/c mice fail to produce the expected immunogenicity outcomes, we will change the dose, mRNA construct (e.g., delete furin cleavage site in S; add two prolines for S stabilization) of the vaccine and/or the delivery strategy.

### **PROGRAM MANAGEMENT**

The contractor shall provide the following as outlined below:

- a) The overall management, integration, and coordination of all contract activities, including a technical and administrative infrastructure to ensure the efficient planning, initiation, implementation, and direction of all contract activities;
- b) A Principal Investigator (PI) or Project Manager (PM) responsible for project management, communication, tracking, monitoring, and reporting on status, progress, and modifications to the project requirements, deliverables and timelines, including projects undertaken by subcontractors;
- c) A PM with responsibility for monitoring and tracking day-to-day progress and timelines of deliverables, coordinating communication and project activities, costs incurred, and program management.
- d) A BARDA liaison (maybe be the PM) with responsibility for effective communication with the Contracting Officer (CO), Contract Specialist (CS), and Contracting Officer's Representative (COR);
- e) Administrative and legal staff capable of developing compliant subcontracts, consulting, and other legal agreements, while also ensuring timely acquisition of all proprietary rights, including intellectual property (IP) rights and reporting all inventions made in the performance of the

contract;

- f) Administrative staff capable of financial management and reporting on all activities conducted by the contractor and any subcontractors;

- g) Contract Review Meetings

The contractor shall participate in regular meetings to coordinate and oversee the contract effort conjointly with the CO, CS, and COR. Such meetings may include, but are not limited to, the following:

- Meeting with the contractors and subcontractors to discuss clinical manufacturing progress, product development, product assay development, scale-up manufacturing development, clinical sample assays development, preclinical/clinical study designs and regulatory issues.
- Meeting with individual contractors and other government officials to discuss the technical, regulatory, and ethical aspects of the program.
- Meeting with technical consultants to discuss technical data provided by the contractor.

- h) The contractor shall participate in teleconferences every month with the CO, CS and COR to discuss the performance of the contract, unless otherwise directed. Teleconferences or additional face-to-face meetings may be more frequent at the request of the CO.

- i) Gantt Chart

Within 30 calendar days of the effective date of the contract, the contractor shall submit a first draft of an updated Gantt Chart to the CO, CS and COR for review. The Gantt Chart shall be incorporated into the contract and will be used to monitor performance. The contractor shall include the key milestones, deliverables, and Go/No-Go decision gates.

- j) Project Management Plan

In the management of this contract, the contractor is encouraged to utilize Project Management tools/techniques to track and monitor the cost and schedule of the project. The contractor and the government agree that at a minimum, the contractor shall utilize the cost and schedule tools/techniques in the contract deliverable for project management purposes.

- k) Risk Management Plan

The contractor shall develop a risk management plan within 90 days of contract award highlighting potential problems or issues that may arise during the life of the contract, including the impact on cost, schedule, and performance. Appropriate remediation plans should reference relevant work segments where appropriate. Updates to this plan shall be included, at a minimum, on a quarterly basis (every three months) in the monthly Project Status Report.

- l) Monthly and Annual Reports

If requested, the contractor shall deliver Project Status Reports on a monthly basis. The reports shall address the items below cross referenced to the SOW or other Project Management Plan tool(s):

- Executive summary highlighting the progress, issues, and relevant manufacturing, non-clinical, clinical, and regulatory activities.

- Progress in meeting contract deliverables, detailing the planned progress and actual progress during the reporting period, explaining any differences between the two and corrective steps.
- Updated Risk Management Plan (every 3 months).
- Three-month rolling forecast of planned activities.
- Progress of regulatory submissions.

m) Data Management

The contractor shall:

- Develop and implement data management and quality control systems/procedures, including transmission, storage, confidentiality, and retrieval of all contract data.
- Provide for the statistical design and analysis of data resulting from the research.
- Provide raw data or specific analyses of data generated with contract funding to the CO, CS, and COR, upon request.

## **REGULATORY**

The contractor shall perform the following as outlined below:

- a) Engage the Food and Drug Administration (FDA) on a path to support the use of the product for the specific indication.
- b) Prepare materials for and requesting, scheduling, and participating in all meetings with the FDA, including meetings to review all data packages.
- c) Provide BARDA with (1) initial draft minutes and final draft minutes of any formal meeting with the FDA, and (2) final draft minutes of any informal meeting with the FDA.

## **FACILITIES, EQUIPMENT, & OTHER RESOURCES**

The contractor shall provide equipment, facilities, and other resources required for implementation of the SOW to comply with all Federal and HHS regulations in:

- a) The humane care and use of vertebrate animals.
- b) The acquisition, handling, storage, and shipment of potentially dangerous biological and chemical agents, including select agents under biosafety levels required for working with the biological agents under study.

## **References:**

Norbert Pardi *et al.* Nucleoside-modified mRNA immunization elicits influenza virus hemagglutinin stalk-specific antibodies. *Nature Communications* 9:3361 (2018)

Pardi, N. et al. Zika virus protection by a single low-dose nucleoside-modified

mRNA vaccination. *Nature* 543, 248–251 (2017).

Kenneth Lundstrom. Latest development on RNA-based drugs and vaccines. *Future Sci. OA* (2018) 4(5)

Yasushi Itoh et al., In vitro and in vivo characterization of new swine-origin H1N1 influenza viruses. *Nature*. 460: 1021–1025 (2009).

Hsieh et al., Structure-based design of prefusion-stabilized SARS-CoV-2 spikes. *Science*. July 23, (2020)

## Attachment 2

### SAMPLE INVOICE REQUEST

<p>(a) Designated Billing Office Name and Address:</p> <p>DHHS/OS/ASPR/BARDA ATTN: Contracting Officer O'Neill House Office Building Washington, DC 20515</p> <p>(b) Contractor's Name:</p> <p>_____</p> <p>Contractor's Address</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>Contractor's EIN: _____</p> <p>Contractor's CAGE: _____</p> <p>Contractor's DUNS: _____</p> <p>Point of Contact Name, Title, Email, Phone:</p> <p>_____</p> <p>_____</p> <p>_____</p> <p>_____</p>	<p>(c) Invoice No.: _____</p> <p>(d) Date Invoice Submitted: _____</p> <p>(e) Contract No.: _____</p> <p>(f) Current Contract Period of Performance:</p> <p>_____</p> <p>(g) Total Price of Contract: _____</p> <p>(h) Total Fixed-Fee (if applicable): _____</p> <p>(i) Invoicing Type: Three-Way Match</p> <p>(j) Office of Acquisitions:</p> <p>DHHS/OS/ASPR/BARDA ATTN: Contracting Officer O'Neill House Office Building Washington, DC 20515</p> <p>(k) Central Point of Distribution: N/A</p>
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(l) This invoicing request represents reimbursable costs for the period from:

CLIN No.	Unit	(m) Current Amount	(n) Cumulative Amount	(o) Total Contract Amount
_____	_____	_____	_____	_____

Brief description of the work/deliverable(s) being invoiced:

I certify that all payments are for appropriate purposes and in accordance with the contract.

(Name of Official)
(Title)

**Note:** Please attach supporting documents and details as specified in the contract to support the work/deliverable(s) being invoiced

### Attachment 3

#### Schedule of Payments

Pursuant to FAR 52.232-2, partial payments will be made upon receipt and acceptance of a deliverable and acceptable invoice for partial delivery of work, as outlined in the table below:

Partial Payment	Deliverable Title	Brief Description of Deliverable	Partial Payment Amount
1	Construction of yeast strains to find the most compatible antigen mRNA VLP producers.  ----- Project Plan	The main objective of Deliverable 1 is to construct yeast strains to find the most compatible antigen mRNA VLP producers  ----- Detailed project plan outlining the goals, deliverables, and intended pathway for the project. This plan should also include a Gantt Chart, Risk Management Plan, and indicate the tools/techniques used to track and monitor the cost and schedule of the project.	\$279,119
2	Completion of in vivo efficacy testing as defined in SOW  ----- (1) Final Report; and  (2) Final Data Package	The main objective of deliverable 2 are to perform and complete in vivo efficacy testing in mice and ferrets to establish the successful candidates' ability to elicit a detectable immune response  ----- (1) Final report to include a summation of the work performed and results obtained for the entire contract period of performance.  (2) Final data package consisting of all raw data produced under this contract. Data may be used by DRIVE for analysis, evaluation, shared with other agencies, or	\$327,661

		shared outside of the government consistent with FAR 52.227-14. This submission package must be delivered in a non-proprietary format.	
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\*The final payment will also include delivery of the (1) Final Report and (2) Final Data Package (outlined in Section F of the contract) This final partial payment will not be paid until all deliverables are received.